<210> 1773 <211> 614 <212> PRT <213> Homo sapiens

<400> 1773 Met Gly Ala Leu Arg Pro Thr Leu Leu Pro Pro Ser Leu Pro Leu Leu 10 Leu Leu Leu Met Leu Gly Met Gly Cys Trp Ala Arg Glu Val Leu Val 25 Pro Glu Gly Pro Leu Tyr Arg Val Ala Gly Thr Ala Val Ser Ile Ser 35 40 Cys Asn Val Thr Gly Tyr Glu Gly Pro Ala Gln Gln Asn Phe Glu Trp Phe Leu Tyr Arg Pro Glu Ala Pro Asp Thr Ala Leu Gly Ile Val Ser 75 70 Thr Lys Asp Thr Gln Phe Ser Tyr Ala Val Phe Lys Ser Arg Val Val 85 Ala Gly Glu Val Gln Val Gln Arg Leu Gln Gly Asp Ala Val Val Leu 105 100 Lys Ile Ala Arg Leu Gln Ala Gln Asp Ala Gly Ile Tyr Glu Cys His 115 120 125 Thr Pro Ser Thr Asp Thr Arg Tyr Leu Gly Ser Tyr Ser Gly Lys Val 140 135 Glu Leu Arg Val Leu Pro Asp Val Leu Gln Val Ser Ala Ala Pro Pro 150 Gly Pro Arg Gly Arg Gln Ala Pro Thr Ser Pro Pro Arg Met Thr Val 165 170 175 His Glu Gly Gln Glu Leu Ala Leu Gly Cys Leu Ala Arg Thr Ser Thr 185 Gln Lys His Thr His Leu Ala Val Ser Phe Gly Arg Ser Val Pro Glu 195 200 205 Ala Pro Val Gly Arg Ser Thr Leu Gln Glu Val Val Gly Ile Arg Ser 215 Asp Leu Ala Val Glu Ala Gly Ala Pro Tyr Ala Glu Arg Leu Ala Ala 235 230 Gly Glu Leu Arg Leu Gly Lys Glu Gly Thr Asp Arg Tyr Arg Met Val 255 250 245 Val Gly Gly Ala Gln Ala Gly Asp Ala Gly Thr Tyr His Cys Thr Ala 270 260 265 Ala Glu Trp Ile Gln Asp Pro Asp Gly Ser Trp Ala Gln Ile Ala Glu 280 275 Lys Arg Ala Val Leu Ala His Val Asp Val Gln Thr Leu Ser Ser Gln 295 300 Leu Ala Val Thr Val Gly Pro Gly Glu Arg Arg Ile Gly Pro Gly Glu 310 315 Pro Leu Glu Leu Leu Cys Asn Val Ser Gly Ala Leu Pro Pro Ala Gly 330 Arg His Ala Ala Tyr Ser Val Gly Trp Glu Met Ala Pro Ala Gly Ala 345 340 Pro Gly Pro Gly Arg Leu Val Ala Gln Leu Asp Thr Glu Gly Val Gly 360 365 355 Ser Leu Gly Pro Gly Tyr Glu Gly Arg His Ile Ala Met Glu Lys Val

375 370 Ala Ser Arg Thr Tyr Arg Leu Arg Leu Glu Ala Ala Arg Pro Gly Asp 395 390 Ala Gly Thr Tyr Arg Cys Leu Ala Lys Ala Tyr Val Arg Gly Ser Gly 410 405 Thr Arg Leu Arg Glu Ala Ala Ser Ala Arg Ser Arg Pro Leu Pro Val 425 420 His Val Arg Glu Glu Gly Val Val Leu Glu Ala Val Ala Trp Leu Ala 445 440 Gly Gly Thr Val Tyr Arg Gly Glu Thr Ala Ser Leu Leu Cys Asn Ile 460 455 Ser Val Arg Gly Gly Pro Pro Gly Leu Arg Leu Ala Ala Ser Trp Trp 475 470 Val Glu Arg Pro Glu Asp Gly Glu Leu Ser Ser Val Pro Ala Gln Leu 490 485 Val Gly Gly Val Gly Gln Asp Gly Val Ala Glu Leu Gly Val Arg Pro 505 500 Gly Gly Gly Pro Val Ser Val Glu Leu Val Gly Pro Arg Ser His Arg 525 520 Leu Arg Leu His Ser Leu Gly Pro Glu Asp Glu Gly Val Tyr His Cys 530 535 540 Ala Pro Ser Ala Trp Val Gln His Ala Asp Tyr Ser Trp Tyr Gln Ala 550 555 545 Gly Ser Ala Arg Ser Gly Pro Val Thr Val Tyr Pro Tyr Met His Ala 575 . 570 565 Leu Asp Thr Leu Phe Val Pro Leu Leu Val Gly Thr Gly Val Ala Leu
580
580
580 580 585 Val Thr Gly Ala Thr Val Leu Gly Thr Ile Thr Cys Cys Phe Met Lys 595 600 . Arg Leu Arg Lys Arg 613 610

<210> 1774 <211> 156 <212> PRT <213> Homo sapiens

<400> 1774 Met Glu Ala Leu Thr Leu Trp Leu Leu Pro Trp Ile Cys Gln Cys Val 10 5 Ser Val Arg Ala Asp Ser Ile Ile His Ile Gly Ala Ile Phe Glu Glu 25 20 Asn Ala Ala Lys Asp Asp Arg Val Phe Gln Leu Ala Val Ser Asp Leu 35 40 Ser Leu Asn Asp Asp Ile Leu Gln Ser Glu Lys Ile Thr Tyr Ser Ile 55 Lys Val Ile Glu Ala Asn Asn Pro Phe Gln Ala Val Gln Glu Ala Cys 75 70 Asp Leu Met Thr Gln Gly Ile Leu Ala Leu Val Thr Ser Thr Gly Cys 65 90 85 Ala Ser Ala Asn Ala Leu Gln Ser Leu Thr Asp Ala Met His Ile Pro 105 110 100 . His Leu Phe Val Gln Arg Asn Pro Gly Gly Ser Pro Arg Thr Ala Cys 120 125 His Leu Asn Pro Ser Pro Asp Gly Glu Ala Tyr Thr Leu Ala Ser Arg WO 01/54477

Pro Pro Val Arg Leu Asn Asp Val Met Leu Arg Leu 145 150 156

> <210> 1775 <211> 896 <212> PRT <213> Homo sapiens

<400> 1775 Met Gln Lys Ala Ser Val Leu Leu Phe Leu Ala Trp Val Cys Phe Leu 10 5 Phe Tyr Ala Gly Ile Ala Leu Phe Thr Ser Gly Phe Leu Leu Thr Arg 1 25 Leu Glu Leu Thr Asn His Ser Ser Cys Gln Glu Pro Pro Gly Pro Gly 40 35 Ser Leu Pro Trp Gly Ser Gln Gly Lys Pro Gly Ala Cys Trp Met Ala 5**5** Ser Arg Phe Ser Arg Val Val Leu Val Leu Ile Asp Ala Leu Arg Phe 75 70 Asp Phe Ala Gln Pro Gln His Ser His Val Pro Arg Glu Pro Pro Val 90 85 Ser Leu Pro Phe Leu Gly Lys Leu Ser Ser Leu Gln Arg Ile Leu Glu 105 100 Ile Gln Pro His His Ala Arg Leu Tyr Arg Ser Gln Val Asp Pro Pro 125 120 Thr Thr Thr Met Gln Arg Leu Lys Ala Leu Thr Thr Gly Ser Leu Pro 140 135 Thr Phe Ile Asp Ala Gly Ser Asn Phe Ala Ser His Ala Ile Val Glu 150 155 Asp Asn Leu Ile Lys Gln Leu Thr Ser Ala Gly Arg Arg Val Val Phe 170 165 Met Gly Asp Asp Thr Trp Lys Asp Leu Phe Pro Gly Ala Phe Ser Lys 185 180 Ala Phe Phe Phe Pro Ser Phe Asn Val Arg Asp Leu Asp Thr Val Asp 205 195 200 Asn Gly Ile Leu Glu His Leu Tyr Pro Thr Met Asp Ser Gly Glu Trp 220 215 Asp Val Leu Ile Ala His Phe Leu Gly Val Asp His Cys Gly His Lys 235 230 His Gly Pro His His Pro Glu Met Ala Lys Lys Leu Ser Gln Met Asp 225 250 245 Gln Val Ile Gln Gly Leu Val Glu Arg Leu Glu Asn Asp Thr Leu Leu 270 265 Val Val Ala Gly Asp His Gly Met Thr Thr Asn Gly Asp His Gly Gly 285 280 275 Asp Ser Glu Leu Glu Val Ser Ala Ala Leu Phe Leu Tyr Ser Pro Thr 300 295 Ala Val Phe Pro Ser Thr Pro Pro Glu Glu Pro Glu Val Ile Pro Gln 315 310 Val Ser Leu Val Pro Thr Leu Ala Leu Leu Gly Leu Pro Ile Pro 330 325 Phe Gly Asn Ile Gly Glu Val Met Ala Glu Leu Phe Ser Gly Gly Glu 345 Asp Ser Gln Pro His Ser Ser Ala Leu Ala Gln Ala Ser Ala Leu His 360 355 Leu Asn Ala Gln Gln Val Ser Arg Phe Phe His Thr Tyr Ser Ala Ala

Thr Gln Asp Leu Gln Ala Lys Glu Leu His Gln Leu Gln Asn Leu Phe Ser Lys Ala Ser Ala Asp Tyr Gln Trp Leu Leu Gln Ser Pro Lys Gly Ala Glu Ala Thr Leu Pro Thr Val Ile Ala Glu Leu Gln Gln Phe Leu Arg Gly Ala Arg Ala Met Cys Ile Glu Ser Trp Ala Arg Phe Ser Leu Val Arg Met Ala Gly Gly Thr Ala Leu Leu Ala Ala Ser Cys Phe Ile Cys Leu Leu Ala Ser Gln Trp Ala Ile Ser Pro Gly Phe Pro Phe Cys Pro Leu Leu Thr Pro Val Ala Trp Gly Leu Val Gly Ala Ile Ala Tyr Ala Gly Leu Leu Gly Thr Ile Glu Leu Lys Leu Asp Leu Val Leu Leu Gly Ala Val Ala Ala Val Ser Ser Phe Leu Pro Phe Leu Trp Lys Ala Trp Ala Gly Trp Gly Ser Lys Arg Pro Leu Ala Thr Leu Phe Pro . 540 , 535 Ile Pro Gly Pro Val Leu Leu Leu Leu Phe Arg Leu Ala Val Phe . 550 Phe Ser Asp Ser Phe Val Val Ala Glu Ala Arg Ala Thr Pro Phe Leu Leu Gly Ser Phe Ile Leu Leu Leu Val Val Gln Leu His Trp Glu Gly Gln Leu Leu Pro Pro Lys Leu Leu Thr Met Pro Arg Leu Gly Thr Ser Ala Thr Thr Asn Pro Pro Arg His Asn Gly Ala Tyr Ala Leu Arg Leu Gly Ile Gly Leu Leu Cys Thr Arg Leu Ala Gly Leu Phe His Arg Cys Pro Glu Glu Thr Pro Val Cys His Ser Ser Pro Trp Leu Ser Pro Leu Ala Ser Met Val Gly Gly Arg Ala Lys Asn Leu Trp Tyr Gly Ala Cys Val Ala Ala Leu Val Ala Leu Leu Ala Ala Val Arg Leu Trp Leu Arg Arg Tyr Gly Asn Leu Lys Ser Pro Glu Pro Pro Met Leu Phe Val Arg Trp Gly Leu Pro Leu Met Ala Leu Gly Thr Ala Ala Tyr Trp Ala Leu Ala Ser Gly Ala Asp Glu Ala Pro Pro Arg Leu Arg Val Leu Val Ser Gly Ala Ser Met Val Leu Pro Arg Ala Val Ala Gly Leu Ala Ala Ser Gly Leu Ala Leu Leu Leu Trp Lys Pro Val Thr Val Leu Val Lys Ala Gly Ala Gly Ala Pro Arg Thr Arg Thr Val Leu Thr Pro Phe Ser Gly Pro Pro Thr Ser Gln Ala Asp Leu Asp Tyr Val Val Pro Gln Ile Tyr Arg His Met Gln Glu Glu Phe Arg Gly Arg Leu Glu Arg Thr Lys Ser Gln Gly Pro Leu Thr Val Ala Ala Tỳr Gln Leu Gly Ser Val Tyr Ser Ala Ala Met Val Thr Ala Leu Thr Leu Leu Ala Phe Pro Leu Leu 

 Leu
 His
 Ala
 Glu
 Arg
 Ile
 Ser
 Leu
 Val
 Phe
 Leu
 Leu
 Phe
 P

<210> 1776 <211> 178 <212> PRT <213> Homo sapiens

<400> 1776 Met Trp Ala Cys Trp Cys Val Leu Gly Thr Pro Gly Val Ala Met Val 1 5 10 Leu Leu His Thr Thr Ile Ser Phe Cys Val Ala Gln Phe Arg Ser Gln 25 20 Leu Leu Thr Trp Leu Cys Ser Leu Leu Leu Leu Ser Thr Leu Arg Leu 45 40 Gln Gly Val Glu Glu Val Lys Arg Arg Trp Tyr Lys Thr Glu Asn Glu 60 55 Tyr Tyr Leu Leu Gln Phe Thr Leu Thr Val Arg Cys Leu Tyr Tyr Thr 75 70 Ser Phe Ser Leu Glu Leu Cys Trp Gln Gln Leu Pro Ala Ala Ser Thr 90 95 85 Ser Tyr Ser Phe Pro Trp Met Leu Ala Tyr Val Phe Tyr Tyr Pro Val 100 105 Leu His Asn Gly Pro Ile Leu Ser Phe Ser Glu Phe Ile Lys Gln Arg 115 120 125 Ser Gln Trp Ser Asn Arg Glu Phe Gly Met Glu Val Glu Ser Lys Gly 135 140 Pro Gly Ala His Pro Pro Gly Phe Glu Ser Leu Leu Cys Phe Gly Leu 145 150 155 Arg Val Leu Ala Glu Leu Leu Thr Leu Leu Met Pro Gln Ser Ser Tyr 165 170 Gln \* 177

<210> 1777 <211> 59 <212> PRT <213> Homo sapiens

50 55 59

<210> 1778 <211> 137 <212> PRT <213> Homo sapiens

<210> 1779 <211> 65 <212> PRT <213> Homo sapiens

<210> 1780 <211> 53 <212> PRT <213> Homo sapiens

<400> 1780

<210> 1781 <211> 109 <212> PRT <213> Homo sapiens

<400> 1781 Met Met His Asn Ile Ile Val Lys Glu Leu Ile Val Thr Phe Phe Leu 5 10 Gly Ile Thr Val Val Gln Met Leu Ile Ser Val Thr Gly Leu Lys Gly 25 20 Val Glu Ala Gln Asn Gly Ser Glu Ser Glu Val Phe Val Gly Lys Tyr 45 40 35 Glu Thr Leu Val Phe Tyr Trp Pro Ser Leu Leu Cys Leu Ala Phe Leu 55 Leu Gly Arg Phe Leu His Met Phe Val Lys Ala Leu Arg Val His Leu 65 70 75 80 Gly Trp Glu Leu Gln Val Glu Glu Lys Ser Val Leu Glu Val His Gln 90 85 Gly Glu His Val Lys Gln Leu Leu Arg Ile Pro Arg Pro 105 100

<210> 1782 <211> 58 <212> PRT <213> Homo sapiens

<210> 1783 <211> 102 <212> PRT <213> Homo sapiens

<400> 1783 Met Leu Ile Pro His Gln Leu Pro Leu Cys Ser Pro Trp Leu Val Gln 10 Ala Met Leu Thr Ile Glu Val Pro Trp Leu Leu Gly Leu Ala His Tyr 25 20 Arg Leu Gly Trp His Ala Leu Glu Gly Ile Phe Trp Trp Gly Ala Ser 40 35 Val Phe His Ala Leu Gln Ala Met Leu Val Arg Lys Trp Pro Leu Gly 55 Leu Val Glu Phe Thr Gly Thr Cys Gly Ile Leu Val Glu Val Ile Gly 75 70 Leu Trp Trp Gly Glu Gly Ser Thr Gly Asn Arg Trp Met Gly Leu Asn 85 Ser Thr Gly Gly Gln \* 100 101

<210> 1784 <211> 243 <212> PRT <213> Homo sapiens

<400> 1784 Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His Leu Leu Val 10 Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala Ala Ala Pro 25 20 Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu Thr Gly Leu 40 35 Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys Gly Asn Leu 60 55 Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp Phe Arg Gly 75 70 Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His Gln Leu Gly 90 8.5 Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Met Thr Asp Asn 100 Lys Thr Gly Glu Val Leu Ile Ser Glu Asn Val Val Ala Ser Ile Gln 120 Pro Ala Glu Gly Ser Phe Glu Gly Asp Leu Lys Val Pro Arg Met Glu 140 135 Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr Asp Ser Phe His 155 150 Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile Lys Leu Pro Arg 170 165 Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His Trp Leu Ser Glu 190 185 180 Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu Arg Lys Gly Thr 205 200 His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser His Ser Arg 220 215 Leu Ser Pro Arg Lys Thr His Leu Leu Tyr Ile Leu Arg Pro Ser Arg 235 Gln Leu 242

<210> 1785 <211> 158 <212> PRT <213> Homo sapiens

<400> 1785 Met Lys Ala Leu Leu Leu Val Leu Pro Trp Leu Ser Pro Ala Asn Tyr Ile Asp Asn Val Gly Asn Leu His Phe Leu Tyr Ser Glu Leu Cys 20 25 Lys Gly Ala Ser His Tyr Gly Leu Thr Lys Asp Arg Lys Arg Arg Ser 35 40 Gln Asp Gly Cys Pro Asp Gly Cys Ala Ser Leu Thr Ala Thr Ala Pro 50 60 Ser Pro Glu Val Ser Ala Ala Thr Ile Ser Leu Met Thr Asp Glu 70 75 80 Pro Gly Leu Asp Asn Pro Ala Tyr Val Ser Ser Ala Glu Asp Gly Gln 90 85 Pro Ala Ile Ser Pro Val Asp Ser Gly Arg Ser Asn Arg Thr Arg Ala 100 1.05 Arg Pro Phe Glu Arg Ser Thr Ile Ile Ser Arg Ser Phe Lys Lys Ile 125 115 120 Asn Arg Ala Leu Ser Val Leu Arg Arg Thr Lys Ser Gly Ser Ala Val 130 135 140 Ala Asn His Ala Asp Gln Gly Arg Glu Asn Ser Glu Asn Thr 155 158

<210> 1786 <211> 142 <212> PRT <213> Homo sapiens

<400> 1786 Met Glu Ser Ala Val Arg Val Glu Ser Gly Val Leu Val Gly Val Val 1 5 10 Cys Leu Leu Leu Ala Cys Pro Ala Thr Ala Thr Gly Pro Glu Val Ala 25 20 Gln Pro Glu Val Asp Thr Thr Leu Gly Arg Val Arg Gly Arg Gln Val 40 Gly Val Lys Gly Thr Asp Arg Leu Val Asn Val Phe Leu Gly Ile Pro 60 Phe Ala Gln Pro Pro Leu Gly Pro Asp Arg Phe Ser Ala Pro His Pro 70 75 Ala Gln Pro Trp Glu Gly Val Arg Asp Ala Ser Thr Ala Pro Pro Met 90 85 Cys Leu Gln Asp Val Glu Ser Met Asn Ser Ser Arg Phe Val Leu Asn 105 110 Gly Lys Gln Gln Ile Phe Ser Val Ser Glu Asp Cys Leu Val Leu Asn 120 125 11.5 Val Tyr Ser Pro Ala Glu Val Pro Ala Gly Ser Gly Arg Pro 140 142 135

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<210> 1787

<211> 120

<212> PRT

<213> Homo sapiens

<221> misc_feature

<222> (1)...(120)

<223> Xaa = any amino acid or nothing
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<400> 1787 Met Ala Leu Thr Gly Tyr, Ser Trp Leu Leu Leu Ser Ala Thr Phe Leu 10 Asn Val Gly Ala Glu Ile Ser Ile Thr Leu Glu Pro Ala Gln Pro Ser 25 Glu Gly Asp Asn Val Thr Leu Val Val His Gly Leu Ser Gly Glu Leu 35 40 Leu Ala Tyr Ser Trp Tyr Ala Gly Pro Thr Leu Ser Val Ser Tyr Leu 55 60 Val Ala Ser Tyr Ile Val Ser Thr Gly Asp Glu Thr Pro Gly Pro Ala 70 His Thr Xaa Arg Glu Ala Val Arg Pro Asp Gly Ser Leu Asp Ile Gln 85 90 95 90 Gly Ile Leu Pro Arg His Ser Ser Thr Tyr Ile Leu Gln Thr Phe Asn 100 105 Arg Gln Leu Gln Thr Glu Val Gly

<210> 1788 <211> 68 <212> PRT <213> Homo sapiens

50 55 Tyr Ile Leu \* 65 67

> <210> 1789 <211> 133 <212> PRT <213> Homo sapiens

<400> 1789
Met Ala Val Val Ile Arg Leu Leu Gly Leu Pro Phe Ile Ala Gly Pro
1 5 10 15

Val Asp Ile Arg His Phe Phe Thr Gly Leu Thr Ile Pro Asp Gly Gly 25 Val His Ile Ile Gly Glu Ile Gly Glu Ala Phe Ile Ile Phe Ala 40 45 Thr Asp Glu Asp Ala Arg Arg Ala Ile Ser Arg Ser Gly Gly Phe Ile 60 55 Lys Asp Ser Ser Val Glu Leu Phe Leu Ser Ser Lys Ala Glu Met Gln 70 75 Lys Thr Ile Glu Met Lys Arg Thr Asp Arg Val Gly Arg Gly Arg Pro 90 85 Gly Ser Gly Thr Ser Gly Val Asp Ser Leu Ser Asn Phe Ile Glu Ser 105 110 100 Val Lys Glu Glu Ala Ser Asn Ser Gly Tyr Gly Ser Ser Ile Asn Gln 125 120 115 Asp Ala Gly Phe His 130 133

<210> 1790 <211> 82 <212> PRT <213> Homo sapiens

<400> 1790 Met Ala Ala Trp Gly Phe Cys Phe Ala Val Ser Ala Leu Val Val Ala 10 Cys Glu Phe Thr Arg Leu His Gly Cys Leu Arg Leu Ser Trp Gly Asn 25 20 Phe Thr Ala Ala Phe Ala Met Leu Ala Thr Leu Leu Cys Ala Thr Ala 45 35 40 Ala Val Leu Tyr Pro Leu Tyr Phe Ala Arg Arg Glu Cys Pro Pro Glu 55 60 Pro Ala Gly Cys Ala Ala Arg Asp Phe Arg Leu Ala Ala Ser Val Phe Ala Gly 82

<210> 1791 <211> 50 <212> PRT <213> Homo sapiens

<210> 1792 <211> 166 <212> PRT <213> Homo sapiens <221> misc\_feature <222> (1)...(166) <223> Xaa = any amino acid or nothing

<400> 1792 Met Leu Leu Trp Leu Leu Leu Ile Leu Thr Pro Gly Arg Glu Gln 10 Ser Gly Val Ala Pro Lys Ala Val Leu Leu Leu Asp Pro Pro Trp Ser 25 20 Thr Ala Phe Lys Gly Glu Lys Val Ala Leu Ile Cys Ser Ser Ile Ser 45 40 35 His Ser Leu Ala Gln Gly Asp Thr Tyr Trp Tyr His Asp Glu Lys Leu 55 Leu Lys Ile Lys His Asp Lys Ile Gln Ile Thr Glu Pro Gly Asn Tyr 75 70 Gln Cys Lys Thr Arg Gly Ser Ser Leu Ser Asp Ala Val His Val Glu 90 85 Phe Ser Pro Asp Trp Leu Ile Leu Gln Ala Leu His Pro Val Phe Glu 110 105 100 Gly Asp Asn Val Ile Leu Arg Cys Gln Gly Lys Asp Asn Lys Asn Thr 115 120 125 His His Lys Val Tyr Tyr Lys Asp Gly Lys Gln Xaa Ser Asn Ser Tyr 140 135 Asn Leu Glu Lys Asn Thr Val Asp Ser Val Ser Arg Asp Asn Ser Pro 145 150 Tyr Tyr Cys Ala Gly \* 165

<210> 1793 <211> 146 <212> PRT <213> Homo sapiens

<400> 1793 Met Ala Thr Ala Ala Gln Gly Pro Leu Ser Leu Leu Trp Gly Trp Leu 15 1.0 Trp Ser Glu Arg Phe Trp Leu Pro Glu Asn Val Ser Trp Ala Asp Leu 25 20 Glu Gly Pro Ala Asp Gly Tyr Gly Tyr Pro Arg Gly Arg His Ile Leu 40 Ser Val Phe Pro Leu Ala Ala Gly Ile Phe Phe Val Arg Leu Leu Phe 60 55 Glu Arg Phe Ile Ala Lys Pro Cys Ala Leu Arg Ile Gly Ile Glu Asp 75 70 Ser Gly Pro Tyr Gln Ala Gln Pro Asn Ala Ile Leu Glu Lys Val Phe 90 85 Ile Ser Ile Thr Lys Tyr Pro Asp Lys Lys Arg Leu Glu Gly Leu Ser 110 105 100 Lys Gln Leu Asp Trp Asn Val Arg Lys Ile Gln Cys Trp Phe Arg His 120 115

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Arg Arg Asn Gln Asp Lys Pro Pro Thr Leu Thr Lys Phe Cys Glu Ser 135 130 145

<210> 1794 <211> 151 <212> PRT <213> Homo sapiens

<400> 1794 Met Glu Arg Arg Leu Leu Gly Gly Met Ala Leu Leu Leu Gln Ala Leu Pro Ser Pro Leu Ser Ala Arg Ala Glu Pro Pro Gln Asp Lys 25 Glu Ala Cys Val Gly Thr Asn Asn Gln Ser Tyr Ile Cys Asp Thr Gly 40 35 His Cys Cys Gly Gln Ser Gln Cys Cys Asn Tyr Tyr Tyr Glu Leu Trp 55 50 Trp Phe Trp Leu Val Trp Thr Ile Ile Ile Ile Leu Ser Cys Cys 75 70 65 Val Cys His His Arg Arg Ala Lys His Arg Leu Gln Ala Gln Gln Arg 85 90 95 Gln His Glu Ile Asn Leu Ile Ala Tyr Arg Glu Ala His Asn Tyr Ser 105 110 100 Ala Leu Pro Phe Tyr Phe Arg Phe Leu Pro Asn Tyr Leu Leu Pro Pro 115 120 125 Tyr Glu Glu Val Val Asn Arg Pro Pro Thr Pro Pro Pro Pro Tyr Ser 135 140 Ala Phe Gln Leu Gln Gln Gln 150 151

<210> 1795 <211> 177 <212> PRT

<213> Homo sapiens

<400> 1795 Met Ala Ala Leu Ala Ala Ala Lys Lys Val Trp Ser Ala Arg Arg . 10 Leu Leu Val Leu Leu Phe Thr Pro Leu Ala Leu Leu Pro Val Val Phe 30 25 Ala Leu Pro Pro Lys Glu Gly Arg Cys Leu Phe Val Ile Leu Leu Met 40 35 Ala Val Tyr Trp Cys Thr Glu Ala Leu Pro Leu Ser Val Thr Ala Leu 60 55 Leu Pro Ile Val Leu Phe Pro Phe Met Gly Ile Leu Pro Ser Asn Lys 65 70 75 80 Val Cys Pro Gln Tyr Phe Leu Asp Thr Asn Phe Leu Phe Leu Ser Gly 90 85 Leu Ile Met Ala Ser Ala Ile Glu Glu Trp Asn Leu His Arg Arg Ile 110 105 100 Ala Leu Lys Ile Leu Met Leu Val Gly Val Gln Pro Ala Arg Leu Ile

Leu Gly Met Met Val Thr Thr Ser Phe Leu Ser Met Trp Leu Ser Asn
130 - - - - - 135 - - - 140 - 140

Thr Ala Ser Thr Ala Met Met Leu Pro Ile Ala Asn Ala Ile Leu Lys
145 - - - - - 150 - - - 150

Ser Leu Phe Gly Gln Lys Glu Val Arg Lys Asp Pro Gln Pro Gly Glu
165 - - - 165 - - - 176

<211> 98
<212> PRT
<213> Homo sapiens
<221> misc\_feature
<222> (1)...(98)
<223> Xaa = any amino acid or nothing

<400> 1796 Met His Pro Leu Pro Gly Tyr Trp Ser Cys Tyr Cys Leu Leu Leu 10 Phe Ser Leu Gly Val Gln Gly Ser Leu Gly Ala Pro Ser Ala Ala Pro 20 25 30 20 Glu Gln Val His Leu Ser Tyr Pro Gly Glu Pro Gly Ser Met Thr Val 40 35 Thr Trp Thr Thr Trp Val Pro Thr Arg Ser Glu Val Gln Phe Gly Leu 60 55 50 Gln Pro Ser Gly Pro Leu Pro Leu Arg Ala Gln Gly Thr Phe Val Pro 75 70 Phe Val Asp Xaa Gly Ile Leu Arg Arg Lys Leu Tyr Ile His Arg Val 90 85 Thr Leu 98

<210> 1797 <211> 96 <212> PRT <213> Homo sapiens

<210> 1796

<400> 1797 Met Phe Leu Trp Leu Phe Leu Ile Leu Ser Ala Leu Ile Ser Ser Thr 10 1 5 Asn Ala Asp Ser Asp Ile Ser Val Glu Ile Cys Asn Val Cys Ser Cys 30 25 20 Val Ser Val Glu Asn Val Leu Tyr Val Asn Cys Glu Lys Val Ser Val 45 40 Tyr Arg Pro Asn Gln Leu Lys Pro Pro Trp Ser Asn Phe Tyr His Leu 60 55 Asn Phe Gln Asn Asn Phe Leu Asn Ile Leu Tyr Pro Asn Thr Phe Leu 75 70 Asn Phe Ser His Ala Val Ser Leu His Leu Gly Asn Asn Lys Leu Gln 95 96 90

<210> 1798 <211> 91 <212> PRT <213> Homo sapiens

<400> 1798 Met Arg Pro Ala Leu Ala Val Gly Leu Val Phe Ala Gly Cys Cys Ser 10 5 1 Asn Val Ile Phe Leu Glu Leu Leu Ala Arg Lys His Pro Gly Cys Gly 25 20 Asn Ile Val Thr Phe Ala Gln Phe Leu Phe Ile Ala Val Glu Gly Phe 40 45 35 Leu Phe Glu Ala Asp Leu Gly Arg Lys Pro Pro Ala Ile Pro Ile Arg 55 60 Tyr Tyr Ala Ile Met Val Thr Met Phe Phe Thr Val Ser Val Val Asn 65 70 Asn Tyr Ala Leu Asn Leu Asn Ile Ala Met Pro 85

<210> 1799 <211> 77 <212> PRT <213> Homo sapiens

 Met Arg Ser Leu Val
 Trp Val
 Leu Ile Gln
 Gln
 Leu Thr
 Pro
 Leu Tyr

 1
 5
 5
 10
 10
 15
 15

 Lys Gly Glu
 Thr
 Trp Thr
 Gln
 Thr
 Glu
 Asp His Val
 Thr
 Met

 Lys Ala Glu
 Ile Arg Val
 Met Leu Leu Glu
 Glu
 Ala Arg Glu
 Asp Cys Gln

 Leu Met Thr
 Lys Arg Ser Gln
 Glu
 Thr
 Gly
 Leu Gln
 Arg Ile Leu Pro

 Glu
 Gly Ser Gln
 Lys Glu
 Pro
 Thr
 Leu Thr
 Thr
 Pro
 \*

 65
 70
 Tro
 Thr
 Leu Thr
 Thr
 Pro
 \*

<210> 1800 <211> 182 <212> PRT <213> Homo sapiens

40 Tyr Phe Asn Ile Phe Ser Arg Ile Leu Gly Gly Ser Gln Val Glu Lys 55 50 Gly Ser Tyr Pro Trp Gln Val Ser Leu Lys Gln Arg Gln Lys His Ile 75 70 Cys Gly Gly Ser Ile Val Ser Pro Gln Trp Val Ile Thr Ala Ala His 85 Cys Ile Ala Asn Arg Asn Ile Val Ser Thr Leu Asn Val Thr Ala Gly 100 105 110 Glu Tyr Asp Leu Ser Gln Thr Asp Pro Gly Glu Gln Thr Leu Thr Ile 120 125 Glu Thr Val Ile Ile His Pro His Phe Ser Thr Lys Lys Pro Met Asp 140 135 Tyr Asp Ile Ala Leu Leu Lys Met Ala Gly Ala Phe Gln Phe Gly His 155 150 Phe Val Gly Pro Ile Cys Leu Pro Glu Leu Arg Glu Gln Phe Glu Ala 170 165 Gly Phe Ile Cys Thr Thr 180 182

<210> 1801 <211> 202 <212> PRT <213> Homo sapiens

<400> 1801 Met Thr Glu Ala Thr Phe Asp Thr Leu Arg Leu Trp Leu Ile Ile Leu Leu Cys Ala Leu Arg Leu Ala Met Met Arg Ser His Leu Gln Ala Tyr 25 Leu Asn Leu Ala Gln Lys Cys Val Asp Gln Met Lys Lys Glu Ala Gly 2.0 45 40 Arg Ile Ser Thr Val Glu Leu Gln Lys Met Val Ala Arg Val Phe Tyr 55 60 Tyr Leu Cys Val Ile Ala Leu Gln Tyr Val Ala Pro Leu Val Met Leu 65 70 75 80 Leu His Thr Thr Leu Leu Leu Lys Thr Leu Gly Asn His Ser Trp Gly 90 85 Ile Tyr Pro Glu Ser Ile Ser Thr Leu Pro Val Asp Asn Ser Leu Leu 105 Ser Asn Ser Val Tyr Ser Glu Leu Pro Ser Ala Glu Gly Lys Met Lys 125 125His Asn Ala Arg Gln Gly Pro Ala Val Pro Pro Gly Met Gln Ala Tyr 135 140 Gly Ala Ala Pro Phe Glu Asp Leu Gln Leu Asp Phe Thr Glu Met Pro 155 150 Lys Cys Gly Asp Leu Ile Pro Arg Phe Gly Leu Pro Leu Arg Ile Gly 170 Ser Asp Asn Gly Leu Ala Phe Val Ala Asp Leu Val Gln Lys Thr Ala 165 185 Lys Trp Lys Gly Pro Gln Ile Val Val Leu 202 200 195

<210> 1802

<211> 172 <212> PRT <213> Homo sapiens

<400> 1802 Met Asn Asn Phe Arg Ala Thr Ile Leu Phe Trp Ala Ala Ala Ala Trp 10 Ala Lys Ser Gly Lys Pro Ser Gly Glu Met Asp Glu Val Gly Val Gln 25 2.0 Lys Cys Lys Asn Ala Leu Lys Leu Pro Val Leu Glu Val Leu Pro Gly 45 35 40 Gly Gly Trp Asp Asn Leu Arg Asn Val Asp Met Gly Arg Val Met Glu 55 Leu Thr Tyr Ser Asn Cys Arg Thr Thr Glu Asp Gly Gln Tyr Ile Ile 70 Pro Asp Glu Ile Phe Thr Ile Pro Gln Lys Gln Ser Asn Leu Glu Met 85 90 Asn Ser Glu Ile Leu Glu Ser Trp Ala Asn Tyr Gln Ser Ser Thr Ser 105 100 Tyr Ser Ile Asn Thr Glu Leu Ser Leu Phe Ser Lys Val Asn Gly Lys 125 120 115 Phe Ser Thr Glu Phe Gln Arg Met Lys Thr Leu Gln Val Lys Asp Gln 140 135 Ala Ile Thr Thr Arg Val Gln Val Arg Asn Leu Val Tyr Thr Val Lys 155 150 Ile Asn Pro Thr Leu Glu Leu Ser Ser Gly Phe Arg 170 172 165

<210> 1803 <211> 158 <212> PRT <213> Homo sapiens

<400> 1803 Met Ser Leu Arg Leu Gly Pro Ala Trp Arg His Leu Thr Cys Leu Gly 5 Thr Lys His Ser Lys Ala Asn Ser Val Leu Ala Ser Gln His Ala Gly 3.0 25 20 Phe Phe Val Ala Gln Gly Arg Trp Ala Ile His Arg Ala Phe Ser Ser 40 35 Arg Thr Ser Pro Thr Pro Pro Arg Gly Pro Leu Leu Pro Gly Arg 60 55 His Pro Leu Leu Ser Arg Arg Arg Ala Gln Ala Ile Arg Ser Ser Thr 70 75 Arg Pro Ser Leu Pro Ala His Leu Phe Lys Pro Ala Pro Ala Ile Ala 90 85 Leu Ile Val Ser Pro Leu Arg Phe Pro Arg Arg Thr Ser Pro Cys His 110 105 100 Leu Ser Gly Pro Pro Ala Pro Pro Cys Arg Thr Leu His Thr Leu Leu 120 125 115 Arg Pro Val Cys Val Val Arg Arg Thr Pro Pro Val Phe Phe Thr Ser 140 135 Phe Thr Pro Ala Arg Ala Ala Val Ala Ser His Pro Thr Pro 155 150

<210> 1804 <211> 102 <212> PRT <213> Homo sapiens

<400> 1804 Met Gly Leu Gly Gln Pro Gln Ala Trp Leu Leu Gly Leu Pro Thr Ala 10 5 Val Val Tyr Gly Ser Leu Ala Leu Phe Thr Thr Ile Leu His Asn Val 25 2.0 Phe Leu Leu Tyr Tyr Val Asp Thr Phe Val Ser Val Tyr Lys Ile Asn 40 35 Lys Met Ala Phe Trp Val Gly Glu Thr Val Phe Leu Leu Trp Asn Ser 60 55 Leu Asn Asp Pro Leu Phe Gly Trp Leu Ser Asp Arg Gln Phe Leu Ser 75 70 Ser Gln Pro Arg Ser Gly Ala Gly Leu Ser Ser Arg Ala Val Leu 90 85 Ala Arg Val Gln Ala Leu 100 102

<210> 1805 <211> 54 <212> PRT <213> Homo sapiens

<210> 1806 <211> 56 <212> PRT <213> Homo sapiens

<210> 1807 <211> 47 <212> PRT <213> Homo sapiens

<210> 1808 <211> 119 <212> PRT <213> Homo sapiens

<400> 1808 Met Ala Ala Ser Leu Leu Ala Val Leu Leu Leu Leu Leu Glu Arg 10 5 Gly Met Phe Ser Ser Pro Ser Pro Pro Pro Ala Leu Leu Glu Lys Val 25 20 Phe Gln Tyr Ile Asp Leu His Gln Asp Glu Phe Val Gln Thr Leu Lys 45 40 Glu Trp Val Ala Ile Glu Ser Asp Ser Val Gln Pro Val Pro Arg Phe 35 55 Arg Gln Glu Leu Phe Arg Met Met Ala Val Ala Ala Asp Thr Leu Gln 65 70 75 80 Arg Leu Gly Ala Arg Val Ala Ser Val Asp Met Gly Pro Gln Gln Leu 85 90 95 Pro Asp Gly Gln Ser Leu Pro Ile Pro Pro Val Ile Leu Ala Glu Leu 105 100 Gly Ser Asp Pro Thr Lys Gly 115

<210> 1809 <211> 91 <212> PRT <213> Homo sapiens

 Met
 Ser
 Arg
 Ser
 His
 Val
 Ala
 Leu
 Leu
 Gly
 Leu
 Ser
 Leu
 Leu
 Met

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 15

 Leu
 Leu
 Tyr
 Ala
 Gly
 Leu
 Pro
 Ser
 Pro
 Pro
 Glu
 Gln
 Thr
 Ser
 Cys

 Leu
 Trp
 Gly
 Asp
 Pro
 Asp
 Val
 Thr
 Val
 Leu
 Ala
 Val
 Ser
 Thr
 Pro
 Ala

 Asn
 Ser
 Pro
 Met
 Phe
 Tyr
 Leu
 Gly
 Leu
 Pro
 Leu
 His
 Leu
 Ala
 His

50 55 60

Arg Val Asp Val Ile Pro Leu Ser Ser Leu Gly Pro Leu Val Ser Pro 65 70 75 80

Leu Arg Cys Gln Ala Leu Pro Pro Arg Leu Ser 90 91

<210> 1810 <211> 58 <212> PRT <213> Homo sapiens

<210> 1811 <211> 48 <212> PRT <213> Homo sapiens

<210> 1812 <211> 84 <212> PRT <213> Homo sapiens

Glu Asp Asn Phe Val Ala Leu Ala Thr Gly Gln Lys Gly Phe Gly Tyr
65 70 75 80
Lys Asn Ser \*
83

<210> 1813 <211> 46 <212> PRT <213> Homo sapiens

<210> 1814 <211> 65 <212> PRT <213> Homo sapiens

<210> 1815 <211> 100 <212> PRT <213> Homo sapiens

65 70 75 80

Pro Asn Ala Ile Pro Phe Ile Val Pro His Pro Gln Thr Gly Pro Asn
85 90 95

Val Arg Cys Ser
100

<211> 115
<212> PRT
<213> Homo sapiens

<221> misc\_feature
<222> (1)...(115)
<223> Xaa = any amino acid or nothing

<210> 1816

<400> 1816 Met Phe Cys Phe Leu Val Ser Val Leu Tyr Ser Lys Ala Lys Leu Ala 10 Ser Ala Cys Gly Gly Ile Ile Tyr Phe Leu Ser Tyr Val Pro Tyr Met 25 20 Tyr Val Ala Ile Arg Glu Glu Val Ala His Asp Lys Ile Thr Ala Phe 45 40 Glu Lys Cys Ile Ala Ser Leu Met Ser Thr Thr Ala Phe Gly Leu Gly 35 55 Ser Lys Tyr Phe Ala Leu Tyr Glu Val Pro Gly Val Gly Ile Gln Trp 50 75 70 His Thr Phe Ser Gln Ser Pro Val Glu Gly Glu Asp Leu Asn Leu Pro 90 85 Pro Pro Pro Pro Met Met Pro Ala Pro Xaa Val Val Tyr Gly Ile Leu 100 105 Thr Lys \* 114

<210> 1817 <211> 144 <212> PRT <213> Homo sapiens

<400> 1817 Met Val Leu Gly Leu Leu Val Gln Ile Trp Ala Leu Gln Glu Ala Ser 10 5 Ser Leu Ser Val Gln Gln Gly Pro Asn Leu Leu Gln Val Arg Gln Gly 30 25 20 Ser Gln Ala Thr Leu Val Cys Gln Val Asp Gln Ala Thr Ala Trp Glu 45 40 Arg Leu Arg Val Lys Trp Thr Lys Asp Gly Ala Ile Leu Cys Gln Pro 5**5** Tyr Ile Thr Asn Gly Ser Leu Ser Leu Gly Val Cys Gly Pro Gln Gly 75 70 Arg Leu Ser Trp Gln Ala Pro Ser His Leu Thr Leu Gln Leu Asp Pro 90 85 Val Ser Leu Asn His Ser Gly Ala Tyr Val Cys Trp Ala Ala Val Glu 105 100

Ile Pro Glu Leu Glu Glu Ala Glu Gly Asn Ile Thr Arg Leu Phe Val
115 - 120 - 125

Asp Pro Asp Asp Pro Thr Gln Asn Arg Asn Arg Ile Ala Ser Phe Pro
130 - 135 - 140 - 140

<210> 1818 <211> 115 <212> PRT <213> Homo sapiens

<400> 1818 Met Gln Ala Asp Arg Gly Gly Val Leu Phe Leu Val Ala Leu Pro Gly
1 5 10 15 Leu Trp Glu Thr Val Leu Arg His Pro Gly Ala Ser Pro Glu Pro Val 25 Ser Leu His Thr Gly Leu Ala Ala Glu Pro Leu Leu Gly Trp Arg Ala 45 35 40 Glu Val Ala Thr Ala Ala Gly Leu Gln Asp Arg Arg Ile Gly Arg Arg 55 Ser Leu Pro Ala Thr Leu Pro Pro Pro Phe Pro Gln Ala Gly Asp Leu 75 70 Arg Glu Ser Ile Leu Leu Leu Pro Cys Arg Glu Ser Arg Ser Thr Ser 85 90 95 Trp Leu Ser Pro Tyr Trp Val Pro Glu Ile Pro Gly Thr Leu His Asp 105 Arg Gly Arg 115

<210> 1819 <211> 70 <212> PRT <213> Homo sapiens

<210> 1820 <211> 635 <212> PRT <213> Homo sapiens

<400> 1820 Met Leu Arg Ser Leu Leu Val Tyr Met Leu Phe Leu Leu Val Thr Leu Leu Ala Ser Tyr Gly Asp Ala Ser Cys His Gly His Ala Tyr Arg Leu Gln Ser Ala Ile Lys Gln Glu Leu His Ser Arg Ala Phe Leu Ala Ile 4.0 Thr Arg Ser Glu Glu Leu Trp Pro Trp Met Ala His Val Leu Leu Pro Tyr Val His Gly Asn Gln Ser Ser Pro Glu Leu Gly Pro Pro Arg Leu Arg Gln Val Arg Leu Gln Glu Ala Leu Tyr Pro Asp Pro Pro Gly Pro Arg Val His Thr Cys Ser Ala Ala Gly Gly Phe Ser Thr Ser Asp Tyr 1.05 Asp Val Gly Trp Glu Ser Pro His Asn Gly Ser Gly Thr Trp Ala Tyr Ser Ala Pro Asp Leu Leu Gly Ala Trp Ser Trp Gly Ser Cys Ala Val Tyr Asp Ser Gly Gly Tyr Val Gln Glu Leu Gly Leu Ser Leu Glu Glu Ser Arg Asp Arg Leu Arg Phe Leu Gln Leu His Asn Trp Leu Asp Asn Arg Ser Arg Ala Val Phe Leu Glu Leu Thr Arg Tyr Ser Pro Ala Val Gly Leu His Ala Ala Val Thr Leu Arg Leu Glu Phe Pro Ala Ala Gly Arg Ala Leu Ala Ala Leu Ser Val Arg Pro Phe Ala Leu Arg Arg Leu Ser Ala Gly Leu Ser Leu Pro Leu Leu Thr Ser Val Cys Leu Leu Leu . 230 Phe Ala Val His Phe Ala Val Ala Glu Ala Arg Thr Trp His Arg Glu Gly Arg Trp Arg Val Leu Arg Leu Gly Ala Trp Ala Arg Trp Leu Leu Val Ala Leu Thr Ala Ala Thr Ala Leu Val Arg Leu Ala Gln Leu Gly Ala Ala Asp Arg Gln Trp Thr Arg Phe Val Arg Gly Arg Pro Arg Arg Phe Thr Ser Phe Asp Gln Val Ala His Val Ser Ser Ala Ala Arg Gly Leu Ala Ala Ser Leu Leu Phe Leu Leu Val Lys Ala Ala Gln His Val Arg Phe Val Arg Gln Trp Ser Val Phe Gly Lys Thr Leu Cys Arg Ala Leu Pro Glu Leu Leu Gly Val Thr Leu Gly Leu Val Val Leu Gly Val Ala Tyr Ala Gln Leu Ala Ile Leu Leu Val Ser Ser Cys Val Asp Ser Leu Trp Ser Val Ala Gln Ala Leu Leu Val Leu Cys Pro Gly Thr . 390 Gly Leu Ser Thr Leu Cys Pro Ala Glu Ser Trp His Leu Ser Pro Leu Leu Cys Val Gly Leu Trp Ala Leu Arg Leu Trp Gly Ala Leu Arg Leu Gly Ala Val Ile Leu Arg Trp Arg Tyr His Ala Leu Arg Gly Glu Leu

Tyr Arg Pro Ala Trp Glu Pro Gln Asp Tyr Glu Met Val Glu Leu Phe 460 455 450 Leu Arg Arg Leu Arg Leu Trp Met Gly Leu Ser Lys Val Lys Glu Phe 475 470 Arg His Lys Val Arg Phe Glu Gly Met Glu Pro Leu Pro Ser Arg Ser 490 495 485 Ser Arg Gly Ser Lys Val Ser Pro Asp Val Pro Pro Pro Ser Ala Gly 500 505 510 Ser Asp Ala Ser His Pro Ser Thr Ser Ser Ser Gln Leu Asp Gly Leu <sup>-</sup> 515 520 525 Ser Val Ser Leu Gly Arg Leu Gly Thr Arg Cys Glu Pro Glu Pro Ser 535 540 Arg Leu Gln Ala Val Phe Glu Ala Leu Leu Thr Gln Phe Asp Arg Leu 555 550 Asn Gln Ala Thr Glu Asp Val Tyr Gln Leu Glu Gln Gln Leu His Ser 565 570 575 Leu Gln Gly Arg Arg Ser Ser Arg Ala Pro Ala Gly Ser Ser Arg Gly 580 585 590 Pro Ser Pro Gly Leu Arg Pro Ala Leu Pro Ser Arg Leu Ala Arg Ala 600 605 Ser Arg Gly Val Asp Leu Ala Thr Gly Pro Ser Arg Thr Pro Leu Arg 610 615 Ala Lys Asn Lys Val His Pro Ser Ser Thr \* 630 625

<210> 1821 <211> 84 <212> PRT <213> Homo sapiens

 Met Gly Ser Thr Trp Gly Ser Pro Gly Trp Val Arg Leu Ala Leu Cys

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 Leu Thr Gly Leu Met Leu Ser Leu Tyr Thr Leu His Val Lys Ala Ala 20
 30

 Arg Ala Arg Asn Arg Asn Tyr Arg Ala Leu Cys Asp Val Gly Thr Val 35
 40
 45

 Ile Ser Cys Thr Arg Val Phe Tyr Ser Lys Leu Pro Ala Asp Thr Leu 50
 55

 Asp Leu Cys Pro Asp Ala Ala Glu Leu Pro Gly Val Ser Arg Trp Phe 65
 70
 75

 Cys Leu Pro Gly 84
 84

<210> 1822 <211> 108 <212> PRT <213> Homo sapiens

PCT/US01/02687 WO 01/54477

25 20 Gly Ser Ala Leu Phe Pro Ser Ala Ala Ala Val Gly Lys Gln Gly Ser 40 45 Met Gly Val Thr Ser His Met Gln Cys Pro Val Cys Gln His Pro Arg Asp Val Leu Leu Ala Ser Pro Val Ser His Ser His Ala Cys Gln Pro 75 70 Gln Pro Ala Gly Cys Ser Asn Cys His Leu Gly His Leu Thr Arg Ser 90 85 Pro Pro Phe Gln Gly Leu Leu Pro Leu Leu Gln \* 105 107 100

<210> 1823 <211> 74 <212> PRT <213> Homo sapiens

<400> 1823 Met Gly Val Val Leu Tyr Val Met Leu Cys Ala Ser Leu Pro Phe Asp 5 10 Asp Thr Asp Ile Pro Lys Met Leu Trp Gln Gln Gln Lys Gly Val Ser 20 25 30 Phe Pro Thr His Leu Ser Ile Ser Ala Asp Cys Gln Asp Leu Leu Lys 35 40 45 Arg Leu Leu Glu Pro Asp Met Ile Leu Arg Pro Ser Ile Glu Glu Val 50 55 Ser Trp His Pro Trp Leu Ala Ser Thr \* 70 73

<210> 1824 <211> 58 <212> PRT <213> Homo sapiens

<400> 1824 Met Ser Leu Ser Cys Thr Gly Phe Ala Leu Glu Lys Arg Cys Ala Gly 10 Trp Val Trp Trp Leu Thr Pro Val Ile Pro Ala Leu Leu Gly Gly Gln
20 25 30 Gly Arg Gln Ile Met Ile Met Val Arg Ser Leu Arg Pro Ala Gly Pro 35 40 Thr Trp Gly Asn Leu Ser Thr Thr Lys Thr 55

<210> 1825 <211> 225 <212> PRT <213> Homo sapiens

<400> 1825

Met Ala Cys Lys Gly Leu Leu Gln Gln Val Gln Gly Pro Arg Leu Pro 10 Trp Thr Arg Leu Leu Leu Leu Leu Val Phe Ala Val Gly Phe Leu 25 2.0 Cys His Asp Leu Arg Ser His Ser Ser Phe Gln Ala Ser Leu Thr Gly 40 35 Arg Leu Leu Arg Ser Ser Gly Phe Leu Pro Ala Ser Gln Gln Ala Cys 60 55 Ala Lys Leu Tyr Ser Tyr Ser Leu Gln Gly Tyr Ser Trp Leu Gly Glu 75 70 Thr Leu Pro Leu Trp Gly Ser His Leu Leu Thr Val Val Arg Pro Ser 90 85 Leu Gln Leu Ala Trp Ala His Thr Asn Ala Thr Val Ser Phe Leu Ser 100 105 Ala His Cys Ala Ser His Leu Ala Trp Phe Gly Asp Ser Leu Thr Ser 125 120 Leu Ser Gln Arg Leu Gln Ile Gln Leu Pro Asp Ser Val Asn Gln Leu 135 130 Leu Arg Tyr Leu Arg Glu Leu Pro Leu Leu Phe His Gln Asn Val Leu 150 155 Leu Pro Leu Trp His Leu Leu Leu Glu Ala Leu Ala Trp Ala Gln Glu 175 165 170 His Cys His Glu Ala Cys Arg Gly Glu Val Thr Trp Asp Cys Met Lys 190 185 180 Thr Gln Leu Ser Glu Ala Val His Trp Thr Trp Leu Cys Leu Gln Asp 205 200 195 Ile Thr Val Ala Phe Leu Asp Trp Ala Leu Ala Leu Ile Ser Gln Gln 220 215 210

<210> 1826 <211> 119 <212> PRT <213> Homo sapiens

Met Tyr Arg Glu Val Cys Ser Ile Arg Phe Leu Phe Thr Ala Val Ser <400> 1826 10 5 Leu Leu Ser Leu Phe Leu Ser Ala Phe Trp Leu Gly Leu Leu Tyr Leu 30 25 Val Ser Pro Leu Glu Asn Glu Pro Lys Glu Met Leu Thr Leu Ser Glu 20 40 Tyr His Glu Arg Ala Arg Ser Gln Gly Gln Gln Leu Leu Gln Phe Gln 35 60 55 Ala Glu Leu Asp Lys Leu His Lys Glu Ala Ser Leu Val Cys Gly Cys 75 70 65 Pro Ser Leu Arg Glu Val Pro Ser Ser Ala Val Ser Arg Leu Glu Pro 90 Pro Ser Ile Ala Gln Pro Leu Leu Ser Arg Leu Gln Leu Tyr Leu Ser . 100 105 Asp Pro Ser Ser Tyr Leu Val 115

<210> 1827 <211> 58 <212> PRT <213> Homo sapiens

<210> 1828 <211> 102 <212> PRT <213> Homo sapiens

<400> 1828 Met Gln Pro Ser Gly Leu Glu Gly Pro Gly Thr Phe Gly Arg Trp Pro 1 5 10 15 Leu Leu Ser Leu Leu Leu Leu Leu Leu Leu Gln Pro Val Thr Cys 25 20 Ala Tyr Thr Thr Pro Gly Pro Pro Arg Ala Leu Thr Thr Leu Gly Ala 40 Pro Arg Ala His Thr Met Pro Gly Thr Tyr Ala Pro Ser Thr Thr Leu 60 55 Ser Ser Pro Ser Thr Gln Gly Leu Gln Glu Gln Ala Arg Ala Leu Met 75 70 Arg Asp Phe Pro Leu Val Asp Gly His Asn Asp Leu Pro Leu Val Leu 90 85 Arg Gln Val Tyr His Asn 100 102

<210> 1829 <211> 88 <212> PRT <213> Homo sapiens

<400> 1829 Met Arg Lys Ile Tyr Thr Thr Val Leu Phe Ala Asn Ile Tyr Leu Ala 1 5 10 Pro Leu Ser Leu Ile Val Ile Met Tyr Gly Arg Ile Gly Ile Ser Leu 25 20 Phe Arg Ala Ala Val Pro His Thr Gly Arg Lys Asn Gln Glu Gln Trp 45 40 35 His Val Val Ser Arg Lys Lys Gln Lys Ile Ile Lys Met Leu Leu Ile 60 55 Val Ala Leu Leu Phe Ile Leu Ser Trp Leu Pro Leu Trp Thr Leu Met 70

Met Leu Ser Asp Tyr Ala Lys Pro 85 88

> <210> 1830 <211> 120 <212> PRT <213> Homo sapiens

<400> 1830 Met Lys Trp Arg Arg Lys Ser Ala Tyr Trp Lys Ala Leu Lys Val Phe 5 10 Lys Leu Pro Val Glu Phe Leu Leu Leu Thr Val Pro Val Val Asp 1 25 20 Pro Asp Lys Asp Asp Gln Asn Trp Lys Arg Pro Leu Asn Cys Leu His Leu Val Ile Ser Pro Leu Val Val Leu Thr Leu Gln Ser Gly Thr 60 55 Tyr Gly Val Tyr Glu Ile Gly Gly Leu Val Pro Val Trp Val Val Val 70 Val Ile Ala Gly Thr Ala Leu Ala Ser Val Thr Phe Phe Ala Thr Ser 65 · 90 Asp Ser Gln Pro Pro Arg Leu His Trp Leu Phe Ala Phe Leu Gly Phe 105 100 Leu Thr Ser Ala Leu Trp Ile Asn 120 115

<210> 1831 <211> 64 <212> PRT <213> Homo sapiens

 <400> 1831

 Met Phe Trp Arg Gly Trp Gly Ala Pro Leu Trp Ala Trp Pro Thr Leu 15

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 1
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 15

 Leu Thr Pro Ile Lys Cys Ser Ser Leu Tyr Asp Ser Phe Phe Ser Pro 20
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<210> 1832 <211> 89 <212> PRT <213> Homo sapiens

WO 01/54477

<210> 1833 <211> 60 <212> PRT <213> Homo sapiens

<210> 1834 <211> 62 <212> PRT <213> Homo sapiens

400- 1024

Met Val Pro Ala Ala Gly Ala Leu Leu Trp Val Leu Leu Leu Asn Leu 15
Gly Pro Arg Ala Ala Gly Ala Gln Gly Leu Thr Gln Thr Pro Thr Glu 30
Met Gln Arg Val Met Leu Arg Phe Gly Cys Ser Val Ile Cys Cys Tyr 45
Cys Ile Ser Val Arg Thr Gly Arg Ser Arg Glu Thr Gly \*
50 55 5 60 61

<210> 1835 <211> 71 <212> PRT <213> Homo sapiens

 Ser Pro Leu Trp Glu Val Val Phe Cys His Thr Pro Cys Phe Arg Ala

 35

 Gln Pro Gln Leu Asp Arg Ala Gly Ser Ser Phe Leu Ile Tyr Pro Ser

 50

 50

 60

 Pro His Ser Thr Ser Asn \*

 65

<210> 1836 <211> 110 <212> PRT <213> Homo sapiens

<400> 1836 Met Leu Met Tyr Met Phe Tyr Val Leu Pro Phe Cys Gly Leu Ala Ala 10 15 5 Tyr Ala Leu Thr Phe Pro Gly Cys Ser Trp Leu Pro Asp Trp Ala Leu 25 Val Phe Ala Gly Gly Ile Gly Gln Ala Gln Phe Ser His Met Gly Ala 40 . 35 Ser Met His Leu Arg Thr Pro Phe Thr Tyr Arg Val Pro Glu Asp Thr 60 55 Trp Gly Cys Phe Phe Val Cys Asn Leu Leu Tyr Ala Leu Gly Pro His 75 70 Leu Leu Ala Tyr Arg Cys Leu Gln Trp Pro Ala Phe Phe His Gln Pro 90 85 Pro Pro Ser Asp Pro Leu Ala Leu His Lys Lys Gln His 105 100

<210> 1837 <211> 91 <212> PRT <213> Homo sapiens

<400> 1837 Met Leu Leu Leu Thr Trp Pro Tyr Ile Leu Leu Gly Phe Leu Phe 10 Cys Ala Phe Val Val Val Asn Gly Gly Ile Val Ile Gly Asp Arg Ser 30 25 20 Ser His Glu Ala Cys Leu His Phe Pro Gln Leu Phe Tyr Phe Phe Ser 40 Phe Thr Leu Phe Phe Ser Phe Pro His Leu Leu Ser Pro Ser Lys Ile 35 60 55 Lys Thr Phe Leu Ser Leu Val Trp Lys Arg Arg Ile Leu Phe Phe Val 75 65 70 Val Thr Leu Val Ser Val Phe Leu Val Trp Asn 90 91

<210> 1838 <211> 201 <212> PRT <213> Homo sapiens

<400> 1838 Met Pro Ile Gly Leu Arg Gly Leu Met Ile Ala Val Met Leu Ala Ala 10 Leu Met Ser Ser Leu Thr Ser Ile Phe Asn Ser Ser Ser Thr Leu Phe 25 Thr Met Asp Ile Trp Arg Arg Leu Arg Pro Arg Ser Gly Glu Arg Glu 45 40 Leu Leu Leu Val Gly Arg Leu Val Ile Val Ala Leu Ile Gly Val Ser 60 55 Val Ala Trp Ile Pro Val Leu Gln Asp Ser Asn Ser Gly Gln Leu Phe 75 70 Ile Tyr Met Gln Ser Val Thr Ser Ser Leu Ala Pro Pro Val Thr Ala 90 85 Val Phe Val Leu Gly Val Phe Trp Arg Arg Ala Asn Glu Gln Gly Ala 110 105 100 Phe Trp Gly Leu Ile Ala Gly Leu Val Val Gly Ala Thr Arg Leu Val 125 120 115 Leu Glu Phe Leu Asn Pro Ala Pro Pro Cys Gly Glu Pro Asp Thr Arg 140 135 Pro Ala Val Leu Gly Ser Ile His Tyr Leu His Phe Ala Val Ala Leu 155 150 Phe Ala Leu Ser Gly Ala Val Val Ala Gly Ser Leu Leu Thr Pro 170 165 Pro Pro Gln Ser Val Gln Ile Glu Asn Leu Thr Trp Trp Thr Leu Ala 185 . 180 Gln Asp Val Pro Leu Gly Thr Lys Ala

<210> 1839
<211> 130
<212> PRT
<213> Homo sapiens
<221> misc\_feature
<222> (1) ... (130)
<223> Xaa = any amino acid or nothing

<400> 1839 Met Leu Phe Phe Leu Gln Ser Leu Phe Met Leu Ala Thr Val Val Leu 10 Tyr Phe Ser His Leu Lys Glu Tyr Val Ala Ser Met Val Phe Ser Leu 25 Ala Leu Gly Trp Thr Asn Met Leu Tyr Tyr Thr Arg Gly Phe Gln Gln 45 35 40 Met Gly Ile Tyr Ala Val Met Ile Glu Lys Met Ile Leu Arg Asp Leu 55 Cys Arg Phe Met Phe Val Tyr Ile Val Phe Leu Phe Gly Phe Ser Thr 75 80 Ala Val Val Thr Leu Ile Glu Asp Gly Lys Asn Asp Ser Leu Pro Ser 90 95 8.5 Glu Ser Thr Ser His Arg Trp Arg Gly Phe Ser Xaa Thr Pro Leu Xaa 105 100 Leu Leu His Lys Leu Tyr Ser Thr Cys Leu Glu Leu Ser Asn Ser Thr 120

Xaa Asp 130

> <210> 1840 <211> 47 <212> PRT <213> Homo sapiens

<210> 1841 <211> 82 <212> PRT <213> Homo sapiens

<400> 1841 Met Thr Ala Arg Leu Met Arg Ser Leu Leu Ala Ala Gln Leu Thr Phe 10 Val Tyr Arg Val Ala His Leu Met Asn Val Ala Gln Arg Ile Arg Gly 30 25 20 Asn Arg Pro Ile Lys Asn Glu Arg Leu Leu Ala Leu Leu Gly Asp Asn 40 35 Glu Lys Met Asn Leu Ser Asp Val Glu Leu Ile Pro Leu Pro Leu Glu 60 50 55 Pro Gln Val Lys Ile Arg Gly Ile Ile Pro Glu Thr Ala Thr Leu Phe 70 75 65 Lys Ser 82

<210> 1842 <211> 77 <212> PRT <213> Homo sapiens

65 70 75 77

<210> 1843 <211> 109 <212> PRT <213> Homo sapiens

<400> 1843 Met Met His Asn Ile Ile Val Lys Glu Leu Ile Val Thr Phe Phe Leu 10 1 5 Gly Ile Thr Val Val Gln Met Leu Ile Ser Val Thr Gly Leu Lys Gly 25 20 Val Glu Ala Gln Asn Gly Ser Glu Ser Glu Val Phe Val Gly Lys Tyr 40 Glu Thr Leu Val Phe Tyr Trp Pro Ser Leu Leu Cys Leu Ala Phe Leu 60 55 50 Leu Gly Arg Phe Leu His Met Phe Val Lys Ala Leu Arg Val His Leu 75 70 Gly Trp Glu Leu Gln Val Glu Glu Lys Ser Val Leu Glu Val His Gln 90 85 Gly Glu His Val Lys Gln Leu Leu Arg Ile Pro Arg Pro 105 100

<210> 1844
<211> 85
<212> PRT
<213> Homo sapiens
<221> misc\_feature
<222> (1)...(85)
<223> Xaa = any amino acid or nothing

<210> 1845 <211> 110 <212> PRT <213> Homo sapiens

<400> 1845 Met Tyr Ala Leu Tyr Ile Thr Val His Gly Tyr Phe Leu Ile Thr Phe 10 Leu Phe Gly Met Val Val Leu Ala Leu Val Val Trp Lys Ile Phe Thr . 30 25 2.0 Leu Ser Arg Ala Thr Ala Val Lys Glu Arg Gly Lys Asn Arg Lys Lys 35 40 Val Leu Thr Leu Leu Gly Leu Ser Ser Leu Val Gly Val Thr Trp Gly 60 55 Leu Ala Ile Phe Thr Pro Leu Gly Leu Ser Thr Val Tyr Ile Phe Ala 75 70 Leu Phe Asn Ser Leu Gln Gly Val Phe Ile Cys Cys Trp Phe Thr Ile 85 90 Leu Tyr Leu Pro Ser Gln Ser Thr Thr Val Ser Ser Ser Thr 105

<210> 1846 <211> 94 <212> PRT <213> Homo sapiens

<400> 1846 Met Thr Glu Pro Pro Gly Ala Ser Ser His Leu Arg Gln Ala Leu Arg 10 5 1 Cys Cys Gln Trp Leu Ala Gly Ile Pro Ser Gln Trp Val Leu Phe Trp 20 25 Glu Val Leu Trp Lys Trp Val Leu Gln Thr Asp Ala Ala Trp Ser Pro 45 40 35 Gly Phe Ser Pro Leu Pro Arg Gly Met Tyr Gln His Pro Ala Leu Pro 60 55 Glu Met Pro Ser Pro Phe Leu Gly Ile Leu Arg Leu Glu Tyr Val Lys 75 70 Leu Leu Gly Leu Cys Met Cys Leu Ser Thr Gly Ser Ser 90 85

<210> 1847 <211> 1300 <212> PRT <213> Homo sapiens

<400> 1847 Met Ala Trp Lys Thr Leu Pro Ile Tyr Leu Leu Leu Leu Ser Val 10 1 Phe Val Ile Gln Gln Val Ser Ser Gln Asp Leu Ser Ser Cys Ala Gly 25 2.0 Arg Cys Gly Glu Gly Tyr Ser Arg Asp Ala Thr Cys Asn Cys Asp Tyr 40 Asn Cys Gln His Tyr Met Glu Cys Cys Pro Asp Phe Lys Arg Val Cys 60 55 Thr Ala Glu Leu Ser Cys Lys Gly Arg Cys Phe Glu Ser Phe Glu Arg 75 70 Gly Arg Glu Cys Asp Cys Asp Ala Gln Cys Lys Lys Tyr Asp Lys Cys

				85	•	•			90					95	
Cys	Pro	Asp	Tyr 100		Ser	Phe	Cys	Ala 105		Val	His	Asn	Pro 110		Ser
Pro	Pro	Ser 115	Ser	Lys	Lys	Ala	Pro 120	Pro	Pro	Ser	Gly	Ala 125	Ser	Gln	Thr
Ile	Lys 130	Ser	Thr	Thr	Lys	Arg 135	Ser	Pro	Lys	Pro	Pro 140	Asn	ГЛа	Lys	ГÀа
Thr 145	Lys	Lys	Val	Ile	Glu 150	Ser	Glu	Glu	Ile	Thr 155	Glu	Glu	His	Ser	Val 160
			Gln	165					170					175	
			Trp 180					185					190		
Glu	Leu	Gln 195	ГЛа	Lys	Leu	Lys	Val 200	Lys	Asp	Asn	Lys	Lys 205	Asn	Arg	Thr
	210		Pro			215					220			-	
225			Asn		230					235					240
			Asn	245					250					255	
			Pro 260					265					270		
		275	Leu 				280					285		-	
	290		Thr			295					300				
305			Lys		310					315					320
			Thr	325					330					335	
			Lys 340					345					350		
		355	Lys				360					365			
	370		Lys			375					380				
385			Ser		390			•		395					400
			Pro Pro	405					410					415	
			420 Ala					425					430		
		435	Ala				440	-	_			445			
	450		Ala			455					460				
465			Pro		470					475					480
				485					490					495	_
			Pro 500 Pro					505					510		
		515	Thr				520					525			-
	530		Thr			535					540			-	
545	110	****	1111	110	550	-LU	FIU	oer	710	555	711T	****	пåз	J. U	560

Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Lys Pro Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Lys Lys Pro Ala Pro Thr Ala Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Thr Ala Pro Thr Thr Pro Lys Lys Leu Thr Pro Thr Thr Pro Glu Lys Leu Ala Pro Thr Thr Pro Glu Lys Pro Ala Pro Thr Thr Pro Glu Glu Leu Ala Pro Thr Thr Pro Glu Glu Pro Thr Pro Thr Thr Pro Glu Glu Pro Ala Pro Thr Thr Pro Lys Ala Ala Ala Pro Asn Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Thr Ala Pro Thr Thr Pro Lys Gly Thr Ala Pro Thr Thr Leu Lys Glu Pro Ala Pro Thr Thr Pro Lys Lys Pro Ala Pro Lys Glu Leu Ala Pro Thr Thr Thr Lys Glu Pro Thr Ser Thr Thr Ser Asp Lys Pro Ala Pro Thr Thr Pro Lys Gly Thr Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Gly Thr Ala Pro Thr Thr Leu Lys Glu Pro Ala Pro Thr Thr Pro Lys Lys Pro Ala Pro Lys Glu Leu Ala Pro Thr Thr Thr Lys Gly Pro Thr Ser Thr Thr Ser Asp Lys Pro Ala Pro Thr Thr Pro Lys Glu Thr Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Lys Pro Ala Pro Thr Thr Pro Glu 835 840 Thr Pro Pro Pro Thr Thr Ser Glu Val Ser Thr Pro Thr Thr Lys B55 Glu Pro Thr Thr Ile His Lys Ser Pro Asp Glu Ser Thr Pro Glu Leu Ser Ala Glu Pro Thr Pro Lys Ala Leu Glu Asn Ser Pro Lys Glu Pro Gly Val Pro Thr Thr Lys Thr Pro Ala Ala Thr Lys Pro Glu Met Thr Thr Thr Ala Lys Asp Lys Thr Thr Glu Arg Asp Leu Arg Thr Thr Pro Glu Thr Thr Ala Ala Pro Lys Met Thr Lys Glu Thr Ala Thr Thr Thr Glu Lys Thr Thr Glu Ser Lys Ile Thr Ala Thr Thr Thr Gln Val Thr Ser Thr Thr Thr Gln Asp Thr Thr Pro Phe Lys Ile Thr Thr Leu Lys Thr Thr Thr Leu Ala Pro Lys Val Thr Thr Lys Lys Thr Ile Thr Thr Thr Glu Ile Met Asn Lys Pro Glu Glu Thr Ala Lys Pro Lys Asp Arg Ala Thr Asn Ser Lys Ala Thr Thr Pro Lys Pro Gln Lys Pro Thr Lys Ala Pro Lys Lys Pro Thr Ser Thr Lys Lys Pro Lys Thr Met

1025 1035 1030 Pro Arg Val Arg Lys Pro Lys Thr Thr Pro Thr Pro Arg Lys Met Thr 1045 1050 1055 Ser Thr Met Pro Glu Leu Asn Pro Thr Ser Arg Ile Ala Glu Ala Met 1060 1065 1070 Leu Gln Thr Thr Arg Pro Asn Gln Thr Pro Asn Ser Lys Leu Val 1075 1080 1085 Glu Val Asn Pro Lys Ser Glu Asp Ala Gly Gly Ala Glu Gly Glu Thr 1090 1095 1100 Pro His Met Leu Leu Arg Pro His Val Phe Met Pro Glu Val Thr Pro 1110 1115 Asp Met Asp Tyr Leu Pro Arg Val Pro Asn Gln Gly Ile Ile Ile Asn 1125 1130 1135 Pro Met Leu Ser Asp Glu Thr Asn Ile Cys Asn Gly Lys Pro Val Asp 1140 1145 1150 Gly Leu Thr Thr Leu Arg Asn Gly Thr Leu Val Ala Phe Arg Gly His Tyr Phe Trp Met Leu Ser Pro Phe Ser Pro Pro Ser Pro Ala Arg Arg 1175 1180 Ile Thr Glu Val Trp Gly Ile Pro Ser Pro Ile Asp Thr Val Phe Thr 1185 1190 1195 1200 Arg Cys Asn Cys Glu Gly Lys Thr Phe Phe Phe Lys Asp Ser Gln Tyr 1205 1210 1215 Trp Arg Phe Thr Asn Asp Ile Lys Asp Ala Gly Tyr Pro Lys Pro Ile 1220 1225 1230 Phe Lys Gly Phe Gly Gly Leu Thr Gly Gln Ile Val Ala Ala Leu Ser 1235 1240 1245 Thr Ala Lys Tyr Lys Asn Trp Pro Glu Ser Val Tyr Phe Phe Lys Arg 1250 1255 1260 Gly Gly Ser Ile Gln Gln Tyr Ile Tyr Lys Gln Glu Pro Val Gln Lys 1265 1270 1275 Cys Pro Gly Arg Arg Pro Ala Leu Asn Tyr Pro Val Tyr Gly Glu Thr 1285 1290 Asp Thr Gly \* 1299

<210> 1848 <211> 103 <212> PRT <213> Homo sapiens

<400> 1848

Met Asn Pro Ala Val Arg Gln Arg Cys Leu Leu Phe Cys Phe Gln Gln 10 1 5 Lys Leu Ile Leu Ser His Phe Phe Leu Leu Gln Val Pro Gln Trp Cys 25 Ala Glu Tyr Cys Leu Ser Ile His Tyr Gln His Gly Gly Val Ile Cys 40 45 35 Thr Gln Val His Lys Gln Thr Val Val Gln Leu Ala Leu Arg Val Ala 55 50 60 Asp Glu Met Asp Val Asn Ile Gly His Glu Val Gly Tyr Val Ile Pro 70 75 Phe Glu Asn Cys Cys Thr Asn Glu Thr Ile Leu Arg Leu Val Cys Gly 85 90 Val Gln Ser Ala Pro Cys \* 100 102

<210> 1849 <211> 50 <212> PRT <213> Homo sapiens

<400> 1849 Wet Ser Arg Phe I

 Met Ser Arg
 Phe Leu Leu Pro Arg
 Glu Gly Cys
 Leu Leu Ile Val Phe
 15

 Met Leu Cys
 Glu Lys
 Thr Leu Pro Phe Leu Phe Thr Leu Lys
 Glu Tyr

 20
 25
 30

 Thr Phe Ile Pro Glu His Arg
 Thr Thr Asp Ile Asn Cys
 Val Asn Thr

 40
 45

 His Glu
 50

<210> 1850 <211> 84 <212> PRT <213> Homo sapiens

<400> 1850 Met Arg Leu His Ser Lys Gly Ser Gln Asp Pro Ser Thr Lys Val His 1 5 1.0 Ile Lys Ala Leu Gln Thr Val Thr Ser Phe Leu Met Leu Phe Ala Ile 20 25 30 Tyr Phe Leu Cys Ile Ile Thr Ser Thr Trp Asn Leu Arg Thr Gln Gln . 35 40 Ser Lys Leu Val Leu Leu Cys Gln Thr Val Ala Ile Met Tyr Pro 55 Ser Phe His Ser Phe Ile Leu Ile Met Gly Ser Arg Lys Leu Lys Gln 65 70 75 Thr Phe Leu Ser

<210> 1851 <211> 51 <212> PRT <213> Homo sapiens

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<210> 1852 <211> 54 <212> PRT <213> Homo sapiens

 <400> 1852

 Met
 Lys
 Thr
 Lys
 Cys
 Lys
 Pro
 Asn
 Ile
 Thr
 Phe
 Phe
 Asn
 Thr
 Ile
 Ile
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 Phe
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<210> 1853 <211> 129 <212> PRT <213> Homo sapiens

<400> 1854

<400> 1853 Met Ala Val Val Arg Val Met Val Val Val Arg Val Thr Ala Val Val 10 Arg Val Met Val Val Val Val Val Val Arg Val Met Val Val 25 20 Val Arg Ile Thr Ala Val Leu Arg Val Met Val Val Arg Ile Met 45 40 Ala Val Ile Arg Val Met Val Val Val Arg Val Thr Ala Ile Val Gly . 55 Val Met Val Val Ile Arg Val Thr Ala Ile Val Ser Ile Met Val Val 75 70 Val Arg Val Met Val Val Val Arg Val Met Val Ala Arg Pro Met 90 85 Val Val Val Arg Val Met Ala Val Val Arg Val Met Ala Asp Ser Ala 110 105 100 Leu Arg Ala Ile Cys Ser Ser Ser Leu Asn Val Thr Phe Ser Leu Glu 125 120 115

<210> 1854
<211> 190
<212> PRT
<213> Homo sapiens
<221> misc\_feature
<222> (1) ... (190)
<223> Xaa = any amino acid or nothing

Met Ser Cys Phe Gly Leu Leu Gly Gly Leu Thr Pro Arg Val Leu 10 Ser Thr Glu Glu Gln Leu Pro Pro Gly Phe Pro Ser Ile Asp Met Gly 25 Pro Gln Leu Lys Val Val Glu Lys Ala Arg Thr Ala Thr Met Leu Cys 45 40 35 Ala Ala Gly Gly Asn Pro Asp Pro Glu Ile Ser Trp Phe Lys Asp Phe 60 55 Leu Pro Val Asp Pro Ala Thr Ser Asn Gly Arg Ile Lys Gln Leu Arg 75 70 Ser Gly Glu Gln Arg Ala Gly Val Lys Gly Pro Cys Arg Pro Gln Asn 90 Lys Arg Leu Val Arg Ser Gln His Ser Leu Leu Pro Trp Ala Trp Ala 110 105 100 Pro Pro Gly Leu Ser Gly Gly Tyr Leu Val Gly Trp Ala Gly Ser Tyr 120 125 115 Cys Arg Cys Ala Trp Leu Arg Glu Glu Ser Ser Trp Leu Ala Val Pro 140 135 Leu Pro Ser Ser Asp Cys Gln Thr Pro Asp Phe Gly Pro Val Leu Pro 155 150 Leu Pro Ala His Val Met Cys Gln Cys Gly Gly Leu Phe Lys Gly Ala 170 Leu Trp Met Leu Thr Leu Leu Leu Pro Cys Xaa Leu Ala \* 185

<210> 1855 <211> 78 <212> PRT <213> Homo sapiens

<210> 1856 <211> 67 <212> PRT <213> Homo sapiens

35 40 45
Thr Leu Met Gly Ser Glu Met Pro Met Ala Leu Ala Ala Glu Thr Trp
50 55 60
Leu Leu \*
65 66

<210> 1857 <211> 107 <212> PRT <213> Homo sapiens

<400> 1857 Met Leu Leu Met Phe Leu Leu Ala Thr Cys Leu Leu Ala Ile Ile Phe 10 Val Pro Gln Glu Met Gln Thr Leu Arg Val Val Leu Ala Thr Leu Gly 20 25 Val Gly Ala Ala Ser Leu Gly Ile Thr Cys Ser Thr Ala Gln Glu Asn 4.5 35 40 Glu Leu Ile Pro Ser Ile Ile Arg Gly Arg Ala Thr Gly Ile Thr Gly 60 55 Asn Phe Ala Asn Ile Gly Gly Ala Leu Ala Ser Leu Val Met Ile Leu 75 70 Ser Ile Tyr Ser Arg Pro Leu Pro Trp Ile Ile Tyr Gly Val Phe Ala 90 85 Ile Leu Ser Gly Leu Val Val Leu Leu Pro 105 107 100

<210> 1858 <211> 134 <212> PRT <213> Homo sapiens

<400> 1858 Met Ile Pro Pro Ala Ile Phe Trp Val Leu Ile Ile Phe Gly Trp Thr 10 5 Leu Val Tyr Gly Phe Val Tyr Phe Thr Thr Gly Glu Thr Ile Met Asp 30 25 Lys Leu Leu Arg Val Leu Tyr Trp Ile Leu Val Lys Thr Phe Phe Arg 40 45 35 Glu Ile Ser Val Ser His Gln Glu Arg Ile Pro Lys Asp Lys Pro Val 60 55 Met Leu Val Cys Ala Pro His Ala Asn Gln Phe Val Asp Gly Met Val 75 70 Ile Ser Thr His Leu Asp Arg Lys Val Tyr Phe Val Gly Ala Ala Ser 85 90 Ser Phe Arg Lys Tyr Lys Val Val Gly Leu Phe Met Lys Leu Met Ala 105 110 Ser Ile Ile Ser Gly Glu Arg His Gln Asp Val Lys Lys Val Leu Thr 120 125 115 Gly Met Ala Thr Glu Lys 134 130

<210> 1859 <211> 82 <212> PRT <213> Homo sapiens

<400> 1859 Met Phe Tyr Val Lys Ala Glu Phe Leu Val Ser Phe Ser Cys Pro Trp 10 Leu Thr Ala Cys Ala Leu Leu Met Ser Cys Ser Trp Phe Leu Thr Leu 25 20 Thr Ile Leu Ser Val Lys Gly Gly Thr Pro Ala Gly Met Leu Asp Gln 40 35 Lys Lys Gly Lys Phe Ala Trp Phe Ser His Ser Thr Glu Thr His Gly 60 55 Asn Val Pro Leu Cys Ser Val Cys Val Asn Ala Cys Gly Cys Ile Pro 70 Asp \* 81

<210> 1860 <211> 46 <212> PRT <213> Homo sapiens

<210> 1861 <211> 128 <212> PRT <213> Homo sapiens

<400> 1861 Met Thr Ile Phe Phe Ser Leu Leu Val Leu Ala Ile Cys Ile Ile Leu 10 Val His Leu Leu Ile Arg Tyr Arg Leu His Phe Leu Pro Glu Ser Val 20 25 30 Ala Val Val Ser Leu Gly Ile Leu Met Gly Ala Val Ile Lys Ile Ile 40 35 Glu Phe Lys Lys Leu Ala Asn Trp Lys Glu Glu Glu Met Phe Arg Pro 55 60 Asn Met Phe Phe Leu Leu Leu Pro Pro Ile Ile Phe Glu Ser Gly 75 70 Tyr Ser Leu His Lys Gly Asn Phe Phe Gln Asn Ile Gly Ser Ile Thr 90 Leu Phe Ala Val Phe Gly Thr Ala Ile Ser Ala Phe Val Val Gly Gly

Gly Ile Tyr Phe Leu Gly Gln Ala His Val Ile Ser Lys Leu Asn Met 115 120 125 128

<210> 1862 <211> 58 <212> PRT <213> Homo sapiens

-

<400> 1862

<210> 1863 <211> 50 <212> PRT <213> Homo sapiens

<210> 1864 <211> 90 <212> PRT <213> Homo sapiens

Gly Val Glu Leu Leu Val Cys Ser Pro Leu Glu Ala Leu Gly Pro Leu 65 70 75 80

Leu Cys Leu Gly Glu Leu Gly Leu Gln Ala 90

<210> 1865 <211> 125 <212> PRT <213> Homo sapiens

<400> 1865 Met Arg Leu Gly Leu Leu Leu Ala Arg His Trp Cys Ile Ala Gly 10 Val Phe Pro Gln Lys Phe Asp Gly Asp Ser Ala Tyr Val Gly Met Ser 25 20 Asp Gly Asn Pro Glu Leu Leu Ser Thr Ser Gln Thr Tyr Asn Gly Gln 45 40 35 Ser Glu Asn Asn Glu Asp Tyr Glu Ile Pro Pro Ile Thr Pro Pro Asn 60 55 Leu Pro Glu Pro Ser Leu Leu His Leu Gly Asp His Glu Ala Ser Tyr 75 70 His Ser Leu Cys His Gly Leu Thr Pro Asn Gly Leu Leu Pro Ala Tyr 90 Ser Tyr Gln Ala Met Asp Leu Pro Ala Ile Met Val Ser Asn Met Leu 105 110 100 Ala Gln Asp Ser His Leu Leu Ser Gly Gln Leu Pro Thr 120 115

<210> 1866 <211> 129 <212> PRT <213> Homo sapiens

<400> 1866 Met Cys Phe Leu Asn Lys Leu Leu Leu Ala Ala Leu Asp Trp Leu 5 Phe Gln Ile Pro Thr Val Pro Glu Asp Leu Phe Phe Leu Glu Glu Gly 25 20 Pro Ser Tyr Ala Phe Glu Val Asp Thr Val Ala Pro Glu His Gly Leu 40 35 Asp Asn Ala Pro Val Val Asp Gln Gln Leu Leu Tyr Thr Cys Cys Pro 60 55 50 Tyr Ile Gly Glu Leu Arg Lys Leu Leu Ala Ser Trp Val Ser Gly Ser 75 70 Ser Gly Arg Ser Gly Gly Phe Met Arg Lys Ile Thr Pro Thr Thr Thr 85 90 Thr Ser Leu Gly Ala Gln Pro Ser Gln Thr Ser Gln Gly Leu Gln Ala 105 Gln Leu Ala Gln Ala Phe Phe His Asn Gln Pro Pro Ser Leu Arg Arg 120 129

<210> 1867 <211> 80 <212> PRT <213> Homo sapiens

<210> 1868 <211> 113 <212> PRT <213> Homo sapiens

<400> 1868 Met Leu Val Trp Leu Tyr Gly Thr Ile Arg Trp Pro Ala Leu Gly Ala 1 5 Pro Arg Trp Trp Pro Trp Val Trp Pro Pro Gly Val Trp Ser Gly Ile 25 20 Glu Thr Pro Ser Ser Thr Pro Arg Ala Arg Ser Leu Arg Gly Thr Gly 40 Gly Ala Val Thr Arg Arg Thr Gly Ser Ser Phe Pro Trp Thr Thr Thr 60 55 Thr Arg Pro Ser Ser Trp Trp Thr Thr Ala His Thr Ala Ala Trp Gly 75 70 Ala Arg Thr Ala Ser Ala Cys Ala Trp Ser Pro Thr Ser His Ser Lys 90 85 Thr Arg Pro Trp Gln Gly Leu Glu Leu Thr Ser Leu Ala Cys Ser Ser 110 112 100

<210> 1869 <211> 72 <212> PRT <213> Homo sapiens

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<210> 1870 <211> 197 <212> PRT <213> Homo sapiens

<400> 1870 Met Arg Thr Leu Leu Thr Ile Leu Thr Val Gly Ser Leu Ala Ala His 10 Ala Pro Glu Asp Pro Ser Asp Leu Leu Gln His Val Lys Phe Gln Ser 30 25 20 Ser Asn Phe Glu Asn Ile Leu Thr Trp Asp Ser Gly Pro Glu Gly Thr 35 40 Pro Asp Thr Val Tyr Ser Ile Glu Tyr Lys Thr Tyr Gly Glu Arg Asp 60 55 Trp Val Ala Lys Lys Gly Cys Gln Arg Ile Thr Arg Lys Ser Cys Asn 75 70 Leu Thr Val Glu Thr Gly Asn Leu Thr Glu Leu Tyr Tyr Ala Arg Val 90 85 Thr Ala Val Ser Ala Gly Gly Arg Ser Ala Thr Lys Met Thr Asp Arg 105 Phe Ser Ser Leu Gln His Thr Thr Leu Lys Pro Pro Asp Val Thr Cys 125 115 120 Ile Ser Lys Val Arg Ser Ile Gln Met Ile Val His Pro Thr Pro Thr 140 135 Pro Ile Arg Ala Gly Asp Gly His Arg Leu Thr Leu Glu Asp Ile Phe 155 160 150 His Asp Leu Phe Tyr His Leu Glu Leu Gln Val Asn Arg Thr Tyr Gln 165 170 175 Met Val Ser Val Cys Cys Thr Leu Val Phe Leu Cys Leu Gly Ser Leu 180 Phe Pro Pro Asn \*

<210> 1871 <211> 75 <212> PRT <213> Homo sapiens

195 196

Arg Glu Ser Arg Ala Cys Ala Pro Gly Glu Arg Pro Asn Phe Leu Gly
50 55 60

Ile Arg Glu Gln Arg Leu Thr Gly Leu Val Val
65 70 75

<210> 1872 <211> 84 <212> PRT <213> Homo sapiens

<400> 1872 Met Pro Phe Ser Thr Cys Thr Ala Leu Pro Ser Trp Ala Thr Leu Ser 1.0 Thr Trp Ser Trp Thr Pro Lys Val Ser Leu Ala Gly Glu Glu Arg Gly 25 20 Glu Thr Cys Gln Pro Asp Pro Phe Pro Pro His Pro Ser Cys Ser Val 45 40 35 Gly Arg Thr Pro Pro His Ser Ser Leu Gly Ser Pro Pro Thr Thr Leu 55 50 Phe Leu Ser Pro Leu Leu Arg Val Glu Ser Arg Gly Ala Lys Cys Val 70 65 Val Cys Cys \* 83

<210> 1873 <211> 51 <212> PRT <213> Homo sapiens

<210> 1874 <211> 503 <212> PRT <213> Homo sapiens

Glu Trp Met Leu Gln His Asp Leu Ile Pro Gly Asp Leu Arg Asp Leu Arg Val Glu Pro Val Thr Thr Ser Val Ala Thr Gly Asp Tyr Ser Ile 55 Leu Met Asn Val Ser Trp Val Leu Arg Ala Asp Ala Ser Ile Arg Leu 75 70 Leu Lys Ala Thr Lys Ile Cys Val Thr Gly Lys Ser Asn Phe Gln Ser 90 95 Tyr Ser Cys Val Arg Cys Asn Tyr Thr Glu Ala Phe Gln Thr Gln Thr 110 105 Arg Pro Ser Gly Gly Lys Trp Thr Phe Ser Tyr Ile Gly Phe Pro Val 120 125 115 Glu Leu Asn Thr Val Tyr Phe Ile Gly Ala His Asn Ile Pro Asn Ala 140 135 Asn Met Asn Glu Asp Gly Pro Ser Met Ser Val Asn Phe Thr Ser Pro 150 155 Gly Cys Leu Asp His Ile Met Lys Tyr Lys Lys Lys Cys Val Lys Ala 170 165 Gly Ser Leu Trp Asp Pro Asn Ile Thr Ala Cys Lys Lys Asn Glu Glu 185 180 Thr Val Glu Val Asn Phe Thr Thr Thr Pro Leu Gly Asn Arg Tyr Met 205 200 Ala Leu Ile Gln His Ser Thr Ile Ile Gly Phe Ser Gln Val Phe Glu 215 220 Pro His Gln Lys Lys Gln Thr Arg Ala Ser Val Val Ile Pro Val Thr 235 230 Gly Asp Ser Glu Gly Ala Thr Val Gln Leu Thr Pro Tyr Phe Pro Thr 250 245 Cys Gly Ser Asp Cys Ile Arg His Lys Gly Thr Val Val Leu Cys Pro 260 265 Gln Thr Gly Val Pro Phe Pro Leu Asp Asn Asn Lys Ser Lys Pro Gly 280 285 275 Gly Trp Leu Pro Leu Leu Leu Ser Leu Leu Val Ala Thr Trp Val 295 300 Leu Val Ala Gly Ile Tyr Leu Met Trp Arg His Glu Arg Ile Lys Lys 310 315 Thr Ser Phe Ser Thr Thr Thr Leu Leu Pro Pro Ile Lys Val Leu Val 330 325 Val Tyr Pro Ser Glu Ile Cys Phe His His Thr Ile Cys Tyr Phe Thr 340 345 Glu Phe Leu Gln Asn His Cys Arg Ser Glu Val Ile Leu Glu Lys Trp 365 360 Gln Lys Lys Lys Ile Ala Glu Met Gly Pro Val Gln Trp Leu Ala Thr 380 375 Gln Lys Lys Ala Ala Asp Lys Val Val Phe Leu Leu Ser Asn Asp Val 395 400 390 Asn Ser Val Cys Asp Gly Thr Cys Gly Lys Ser Glu Gly Ser Pro Ser 410 405 Glu Asn Ser Gln Asp Leu Phe Pro Leu Ala Phe Asn Leu Phe Cys Ser 425 Asp Leu Arg Ser Gln Ile His Leu His Lys Tyr Val Val Val Tyr Phe 445 440 435 Arg Glu Ile Asp Thr Lys Asp Asp Tyr Asn Ala Leu Ser Val Cys Pro 455 Lys Tyr His Leu Met Lys Asp Ala Thr Ala Phe Cys Ala Glu Leu Leu 475 470 His Val Lys Gln Gln Val Ser Ala Gly Lys Arg Ser Gln Ala Cys His 490 485 Asp Gly Cys Cys Ser Leu \*

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500 502

<210> 1875
<211> 158
<212> PRT
<213> Homo sapiens
<221> misc\_feature
<222> (1) ... (158)
<223> Xaa = any amino acid or nothing

<400> 1875 Met Xaa Pro Pro Thr Arg Pro Arg Thr Arg Gly Val Gly Ile Phe Tyr 10 5 Phe Val Ile Tyr Ile Ile Ile Ser Phe Leu Val Val Val Asn Met Tyr 20 25 30 Ile Ala Val Ile Leu Glu Asn Phe Ser Val Ala Thr Glu Glu Ser Thr 40 35 Glu Pro Leu Ser Glu Asp Asp Phe Glu Met Phe Tyr Glu Val Trp Glu 55 Lys Phe Asp Pro Asp Ala Thr Gln Phe Ile Glu Phe Ser Lys Leu Ser 75 70 Asp Phe Ala Ala Leu Asp Pro Pro Leu Leu Ile Ala Lys Pro Asn 90 85 Lys Val Gln Leu Ile Ala Met Asp Leu Pro Met Val Ser Gly Asp Arg 110 105 100 Ile His Cys Leu Asp Ile Leu Phe Ala Phe Thr Lys Arg Val Leu Gly 120 Glu Ser Gly Glu Met Asp Ser Leu Arg Ser Gln Met Glu Glu Arg Phe 115 · 140 135 Met Ser Ala Asn Pro Ser Lys Val Ser Tyr Glu Pro Ile Thr 155 150

<210> 1876 <211> 106 <212> PRT <213> Homo sapiens

<400> 1876 Met Gly Asn Arg Ala Val Ile Ile Ala Arg Gln Leu Ser Ser Val His 10 5 Thr Leu Ile Cys Asn Phe Phe Trp Leu Leu Leu Arg Thr Thr Gly Gly 25 Asp Leu Asp Ser Leu Lys Cys Ser Tyr Glu Ser Ile Gly Leu Asn Ser 20 40 Ile Ser Thr His Glu Phe Ile Cys Thr Trp Gln Arg Arg Leu Asn Phe 60 55 Ser Phe Val Met Ser Phe Lys Pro Leu Phe Arg Ala Ser Pro His Ser 50 75 70 Tyr Leu Leu Ile Ile Gly Ser Gln Leu His Glu Thr Phe Asn Leu Gly 90 85 Ser Ile Ser Ser Glu Glu Lys Cys Ser \* 100

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<210> 1877
<211> 241
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(241)
<223> Xaa = any amino acid or nothing
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<400> 1877 Met Leu Trp Ala Leu Trp Pro Arg Trp Leu Ala Asp Lys Met Leu Pro 10 1 Leu Leu Gly Ala Val Leu Leu Gln Lys Arg Glu Lys Arg Gly Pro Leu 25 20 Trp Arg His Trp Arg Arg Glu Thr Tyr Pro Tyr Tyr Asp Leu Gln Val 45 35 Lys Val Leu Arg Ala Thr Asn Ile Arg Gly Thr Asp Leu Leu Ser Lys 60 55 50 Ala Asp Cys Tyr Val Gln Leu Trp Leu Pro Thr Ala Ser Pro Ser Pro 75 70 Ala Gln Thr Arg Ile Val Ala Asn Cys Ser Asp Pro Glu Trp Asn Glu 90 85 Thr Phe His Tyr Gln Ile His Gly Ala Val Lys Asn Val Leu Glu Leu 100 105 110 Thr Leu Tyr Asp Lys Asp Ile Leu Gly Ser Asp Gln Leu Ser Leu Leu 115 120 125 Leu Phe Asp Leu Arg Ser Leu Lys Cys Gly Gln Pro His Lys His Thr 135 140 Phe Pro Leu Asn His Gln Asp Ser Gln Glu Leu Gln Val Glu Phe Val 155 160 150 Leu Glu Lys Ser Gln Glu Pro Ala Ser Glu Val Ile Thr Asn Gly Val 165 170 175 Leu Gly Ala His Pro Trp Leu Arg Met Lys Gly Met Ile Leu Gly Glu 190 180 185 Gly Arg Ala Pro Arg Gln Gln His Gly Gln Ser Trp Glu Gly Gly Val 205 195 200 Gly Pro Ser Pro Leu Ser Xaa Xaa Xaa Asn Thr Gly Gly Lys Ile Val 210 215 220 Gly Phe Trp Glu Glu Met Ala Asn Gly Thr Gly Ala Pro Pro Arg Pro 230 225 Pro 241

<210> 1878 <211> 50 <212> PRT <213> Homo sapiens

20 25 30

Val Gly Glu Gln Thr Lys Gly Lys Ser Asn Arg Val Leu Pro Val Phe
35 40 45

Leu \*
49

<210> 1879 <211> 56 <212> PRT <213> Homo sapiens

<210> 1880
<211> 161
<212> PRT
<213> Homo sapiens
<221> misc\_feature
<222> (1)...(161)
<223> Xaa = any amino acid or nothing

<400> 1880 Met Pro Ser Ala Ser Leu Leu Val Asn Leu Leu Ser Ala Leu Leu Ile 15 10 5 Leu Phe Val Phe Gly Glu Thr Glu Ile Arg Phe Thr Gly Gln Thr Glu 25 20 Phe Val Val Asn Glu Thr Ser Thr Thr Val Ile Arg Leu Ile Ile Glu 40 Arg Ile Gly Glu Pro Ala Asn Val Thr Ala Ile Val Ser Leu Tyr Gly 60 55 Glu Asp Ala Gly Asp Phe Phe Asp Thr Tyr Ala Ala Ala Phe Ile Pro 75 70 Ala Gly Glu Thr Asn Arg Thr Val Tyr Ile Ala Val Cys Asp Asp Asp 90 85 Leu Pro Glu Pro Asp Glu Thr Phe Ile Phe His Leu Thr Leu Gln Lys 105 Pro Ser Ala Asn Val Lys Leu Gly Trp Pro Arg Thr Val Thr Val Thr 120 Ile Leu Ser Asn Gly Gln Met Ala Phe Trp Glu Phe Ile Phe Ile Leu 135 140 Asn Ile Gly Leu Pro Pro Pro Ile Pro Pro Ser Gly Xaa Leu Lys Ala 155 150 Pro 161

<210> 1881 <211> 130 <212> PRT <213> Homo sapiens

<400> 1881 Met Gly Ile Tyr Gln Met Tyr Leu Cys Phe Leu Leu Ala Val Leu Leu 10 Gln Leu Tyr Val Ala Thr Glu Ala Ile Leu Ile Ala Leu Val Gly Ala 25 Thr Pro Ser Tyr His Trp Asp Leu Ala Glu Leu Leu Pro Asn Gln Ser 35 40 His Gly Asn Gln Ser Ala Gly Glu Asp Gln Ala Phe Gly Asp Trp Leu 55 60 Leu Thr Ala Asn Gly Ser Glu Ile His Lys His Val His Phe Ser Ser 70 Ser Phe Thr Ser Ile Ala Ser Glu Trp Phe Leu Ile Ala Asn Arg Ser 90 Tyr Lys Val Ser Ala Ala Ser Ser Phe Phe Phe Ser Gly Val Phe Val 100 105 110 Gly Val Ile Ser Phe Gly Gln Leu Ser Asp Arg Phe Gly Arg Lys 120 Val Tyr 130

<210> 1882 <211> 108 <212> PRT <213> Homo sapiens

<400> 1882

Asn Pro Cys Ile Met Cys Val Cys Leu Asn Lys Glu Val Thr Cys Lys 65 70 75 80
Arg Glu Lys Cys Pro Val Leu Ser Arg Asp Cys Ala Leu Ala Ile Lys 85 90 95

Gln Arg Gly Ala Cys Cys Glu Gln Cys Lys Gly Cys 100 105 108

> <210> 1883 <211> 88 <212> PRT <213> Homo sapiens

<400> 1883 Met Leu Phe Tyr Leu Val Ser Val Cys Leu Cys Val Ala Val Ile Val 5 Ala Phe Gln Leu Thr Ala Phe Thr Phe Arg Lys Asn Leu Ala Ala Thr 25 Ala Leu Leu Leu Ser Leu Phe Gly Tyr Ala Thr Leu Pro Trp Met Tyr 40 45 35 Leu Met Ser Arg Ile Phe Ser Ser Ser Asp Val Ala Phe Ile Ser Tyr 50 55 Val Ser Leu Asn Phe Ile Phe Gly Leu Cys Thr Met Leu Ile Thr Ile **7**5 65 70 Met Pro Arg Leu Leu Ala Ile Ile 85 88

<210> 1884 <211> 116 <212> PRT <213> Homo sapiens

<400> 1884 Met Cys Trp Ala Arg Cys Trp Thr Arg Trp Asn Thr Cys Thr Ile Trp 1 5 10 15 Thr Ser Ser Thr Asp Pro Phe Arg Lys Cys Trp Met Ala Pro Glu Ala 20 Leu Asn Phe Ser Phe Ser His Lys Ser Asp Ile Trp Ser Leu Gly Cys 35 40 Ile Ile Leu Asp Met Thr Ser Cys Ser Phe Met Asp Gly Thr Glu Ala 60 55 Met His Leu Arg Lys Ser Leu Arg Gln Ser Pro Gly Ser Leu Lys Ala 75 70 65 Val Leu Lys Thr Met Glu Glu Lys Gln Ile Pro Asp Val Glu Thr Phe 95 **8**5 90 Arg Asn Leu Leu Pro Leu Met Leu Gln Ile Asp Pro Ser Asp Arg Ile 105 100 Thr Ile Lys \* 115

<210> 1885 <211> 115 <212> PRT <213> Homo sapiens

<210> 1886 <211> 357 <212> PRT <213> Homo sapiens

<400> 1886 Met Ile Leu Ser Leu Leu Phe Ser Leu Gly Gly Pro Leu Gly Trp Gly 5 10 Leu Leu Gly Ala Trp Ala Gln Ala Ser Ser Thr Ser Leu Ser Asp Leu 20 25 Gln Ser Ser Arg Thr Pro Gly Val Trp Lys Ala Glu Ala Glu Asp Thr 45 40 Gly Lys Asp Pro Val Gly Arg Asn Trp Cys Pro Tyr Pro Met Ser Lys 55 60 Leu Val Thr Leu Leu Ala Leu Cys Lys Thr Glu Lys Phe Leu Ile His 75 70 Ser Gln Gln Pro Cys Pro Gln Gly Ala Pro Asp Cys Gln Lys Val Lys 85 90 Val Met Tyr Arg Met Ala His Lys Pro Val Tyr Gln Val Lys Gln Lys 100 105 110 Val Leu Thr Ser Leu Ala Trp Arg Cys Cys Pro Gly Tyr Thr Gly Pro 115 120 125 Asn Cys Glu His His Asp Ser Met Ala Ile Pro Glu Pro Ala Asp Pro 130 135 140 Gly Asp Ser His Gln Glu Pro Gln Asp Gly Pro Val Ser Phe Lys Pro 150 155 Gly His Leu Ala Ala Val Ile Asn Glu Val Glu Val Gln Gln Glu Gln 170 165 Gln Glu His Leu Leu Gly Asp Leu Gln Asn Asp Val His Arg Val Ala 190 185 Asp Ser Leu Pro Gly Leu Trp Lys Ala Leu Pro Gly Asn Leu Thr Ala 200 205 195 Ala Val Met Glu Ala Asn Gln Thr Gly His Glu Phe Pro Asp Arg Ser 220 215 Leu Glu Gln Val Leu Leu Pro His Val Asp Thr Phe Leu Gln Val His 230 235 Phe Ser Pro Ile Trp Arg Ser Phe Asn Gln Ser Leu His Ser Leu Thr 250 . 255 245 Gln Ala Ile Arg Asn Leu Ser Leu Asp Val Glu Ala Asn Arg Gln Ala 270 265 Ile Ser Arg Val Gln Asp Ser Ala Val Ala Arg Ala Asp Phe Gln Glu 285 275 280 Leu Gly Ala Lys Phe Glu Ala Lys Val Gln Glu Asn Thr Gln Arg Val 295 300 Gly Gln Leu Arg Gln Asp Val Glu Asp Arg Leu His Ala Gln His Phe 310 315 Thr Leu His Arg Ser Ile Ser Glu Leu Gln Ala Asp Val Asp Thr Lys

Leu Lys Arg Leu His Lys Ala Gln Glu Ala Pro Gly Thr Asn Gly Ser 335 Leu Val Leu Glu Arg . 325 - 325 - 336 - 335

<210> 1887 <211> 86 <212> PRT <213> Homo sapiens

<400> 1887 Met Leu Cys Ser Arg Leu Gly Thr Thr Ala Ser Trp Arg Arg Leu Gly 10 Ile Arg Ala Trp Ala Pro Leu Leu Leu Phe Pro Trp Asp Trp His 25 20 Phe Ile Leu Ser Phe Ser Ser Arg Pro Trp Ala Gly Thr Leu Leu Ala 35 40 45 Pro His Asp Val Ile Met Gly Ser Ser Thr Phe Pro Gln Ser Cys Gln 55 60 Ala Glu Ala Gly Pro Arg His Ala Trp Pro Thr Gly Arg Phe Ser Arg Arg Leu Arg Arg Val \* 85

<210> 1888 <211> 48 <212> PRT

<213> Homo sapiens

<210> 1889 <211> 79 <212> PRT <213> Homo sapiens

Asn Gln Thr Phe Leu Cys Leu Leu Ser Thr Thr Ala Phe Gly Gln Gly 50 55 60

Val Phe Phe Ile Thr Phe Leu Glu Gly Gln Glu Thr Gly Ile His 65 70 75 79

<210> 1890 <211> 251 <212> PRT <213> Homo sapiens

<400> 1890 Met Asn Val Ile Tyr Phe Pro Leu His Leu Phe Val Val Tyr Ser Arg 1 5 10 15 Ala Tyr Thr Ser Leu Val Leu Val Gly Cys Thr Asn Leu Cys Ala Val 20 25 Leu Phe Ala Arg Cys Leu Asp Asp His Leu Val Ser Leu Arg Met Ser 40 35 Gly Ser Arg Lys Glu Phe Asp Val Lys Gln Ile Leu Lys Ile Arg Trp Arg Trp Phe Gly His Gln Ala Ser Ser Pro Asn Ser Thr Val Asp Ser 75 70 Gln Gln Gly Glu Phe Trp Asn Arg Gly Gln Thr Gly Ala Asn Gly Gly 90 85 Arg Lys Phe Leu Asp Pro Cys Ser Leu Gln Leu Pro Leu Ala Ser Ile 100 105 110 Gly Tyr Arg Arg Ser Ser Gln Leu Asp Phe Gln Asn Ser Pro Ser Trp 115 120 125 Pro Met Ala Ser Thr Ser Glu Val Pro Ala Phe Glu Phe Thr Ala Glu 135 140 Asp Cys Gly Gly Ala His Trp Leu Asp Arg Pro Glu Val Asp Asp Gly 145 150 155 Thr Ser Glu Glu Glu Asn Glu Ser Asp Ser Ser Ser Cys Arg Thr Ser 165 170 175 Asn Ser Ser Gln Thr Leu Ser Ser Cys His Thr Met Glu Pro Cys Thr 180 185 190 Ser Asp Glu Phe Phe Gln Ala Leu Asn His Ala Glu Gln Thr Phe Lys 200 205 195 Lys Met Glu Asn Tyr Leu Arg His Lys Gln Leu Cys Asp Val Ile Leu 210 215 220 Val Ala Gly Asp Arg Arg Ile Pro Ala His Arg Leu Val Leu Ser Ser 225 230 235 Val Ser Asp Tyr Phe Ala Gly Met Phe Thr Asn 250 251 245

<210> 1891 <211> 117 <212> PRT <213> Homo sapiens <221> misc\_feature

<221> misc\_feature
<222> (1)...(117)
<223> Xaa = any amino acid or nothing

<400> 1891 Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu Phe Ala Xaa Trp Met 10 Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu Arg Gln Asn Glu Gln 20 Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr Glu Pro Tyr Leu Ala 40 Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly Thr Thr Tyr Asp Phe 60 55 Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys Pro Leu Cys Val Glu 70 Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu Trp Ile Thr Ile Pro 90 85 Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile Leu Leu Val Asn Leu 105 100 Leu Val Ala Met Phe 115 117

<210> 1892 <211> 103 <212> PRT <213> Homo sapiens

<400> 1892 Met Leu Cys His Pro His Val His His Leu Val Cys Leu Leu Ala 1 5 10 Thr Leu Thr Phe Ser Leu Asn Ala Ser Cys Ala Glu Gln Thr Phe His 25 20 Ser Gln Gln Ser Asn Gly Glu Phe Met Ala Thr Leu Pro Ser Ile Ser 40 35 Lys Gln Phe Gly Val Ile Val Trp Lys Pro Gln Arg Lys Asp Val Ile 60 55 Arg Leu Pro Val Ala Leu Ser Phe Ser Ser Gly Ala Arg Leu Ala Phe 75 70 Thr Cys Leu Arg Lys Ile Ser Gly Phe Arg Ala Leu Ile Trp Gly Glu 90 85 Asp Lys Gly Trp Asp Leu 100 102

<210> 1893
<211> 77
<212> PRT
<213> Homo sapiens
<221> misc\_feature
<222> (1)...(77)
<223> Xaa = any amino acid or nothing

Ala Leu Val Phe Leu Leu Leu Val Gly Leu Leu Asn Ala Arg Gly Ile
35 40 45

Lys Glu Ser Met Arg Ala Xaa Val Val Met Thr Val Val Glu Val Thr
50 55 60

Gly Leu Val Leu Val Val Val Leu Ala Leu Val Pro Gly
65 70 77

<210> 1894 <211> 46 <212> PRT <213> Homo sapiens

<210> 1895 <211> 162 <212> PRT <213> Homo sapiens

<400> 1895 Met Thr Ala Trp Arg Arg Phe Gln Ser Leu Leu Leu Leu Gly Leu 10 Leu Val Leu Cys Ala Arg Leu Leu Thr Ala Ala Lys Gly Gln Asn Cys 20 25 Gly Gly Leu Val Gln Gly Pro Asn Gly Thr Ile Glu Ser Pro Gly Phe 4.5 40 35 Pro His Gly Tyr Pro Asn Tyr Ala Asn Cys Thr Trp Ile Ile Ile Thr 50 55 60 Gly Glu Arg Asn Arg Ile Gln Leu Ser Phe His Thr Phe Ala Leu Glu 65 70 75 Glu Asp Phe Asp Ile Leu Ser Val Tyr Asp Gly Gln Pro Gln Gln Gly 90 85 Asn Leu Lys Val Arg Leu Ser Gly Phe Gln Leu Pro Ser Ser Ile Val 105 110 100 Ser Thr Gly Ser Ile Leu Thr Leu Trp Phe Thr Thr Asp Phe Ala Val 120 125 115 Ser Ala Gln Gly Phe Lys Ala Leu Tyr Glu Gly Arg Arg Leu Val Val 130 135 140 Phe Cys Thr Cys Ile His Cys Pro Asn Asp Leu Ile His Ala Thr Leu 150 Asp \* 161

<210> 1896 <211> 60

<212> PRT <213> Homo sapiens

<210> 1897 <211> 49 <212> PRT <213> Homo sapiens

<210> 1898 <211> 52 <212> PRT <213> Homo sapiens

<210> 1899 <211> 112 <212> PRT <213> Homo sapiens

<400> 1899

Met Ala Ile Pro Ser Val Val Ile Ser Gly Leu Ala Val Leu Leu Val 5 10 Ala Met Ala Leu Pro Ser Leu Ser Gly Ser Glu Ala Ile Lys Ser Met 25 20 Thr Ile Pro Gly Leu Val Val Pro Thr Val Val Arg Phe Met Ala Val 40 Pro Gly Leu Ile Val Pro Ala Val Ala Lys Phe Thr Val Leu Pro Asp 55 Leu Thr Val Pro Thr Glu Asp Lys Ser Leu Ala Val Pro Ser Leu Ile 70 75 Ser Arg Ala Gly Asn Ser Val Pro Val Ser Ser Trp Asp Val Phe Gly 85 90 Val Ala Lys Leu Ile Ala Lys Leu Gly Leu Leu Ala Ala Ile Val Ala 105

<210> 1900 <211> 128 <212> PRT <213> Homo sapiens

<400> 1900

Met Arg Val Tyr Gly Thr Cys Thr Leu Val Leu Met Ala Leu Val Val 1 10 Phe Val Gly Val Lys Tyr Val Asn Lys Leu Ala Leu Val Phe Leu Ala Cys Val Val Leu Ser Ile Leu Ala Ile Tyr Ala Gly Val Ile Lys Ser Ala Phe Asp Pro Pro Asp Ile Pro Val Cys Leu Leu Gly Asn Arg Thr 55 60 Leu Ser Arg Arg Ser Phe Asp Ala Cys Val Lys Ala Tyr Gly Ile His 70 75 Asn Asn Ser Ala Thr Ser Ala Leu Trp Gly Leu Phe Cys Asn Gly Ser 90 85 9.5 Gln Pro Ser Ala Ala Cys Asp Glu Tyr Phe Ile Gln Asn Asn Val Thr 105 100 110 Glu Ile Gln Gly Ile Pro Gly Ala Ala Ser Gly Val Phe Leu Glu Asn 120

<210> 1901 <211> 68 <212> PRT <213> Homo sapiens

<400> 1901 Met Glu Leu Leu Leu Leu Leu Thr Cys Phe Ser Glu Ala Met Tyr 1 5 10 Leu Pro Pro Ala Pro Glu Ser Gly Ser Thr Asn Pro Trp Val Gln Phe 2.0 25 Phe Cys Ser Thr Glu Asn Arg His Ala Leu Pro Leu Phe Thr Ser Leu

35 40 45

Leu Asn Thr Val Cys Ala Tyr Asp Pro Val Glu Tyr Gly Ile Pro Tyr
50 55 60

Asn His Leu Tyr
65 68

<210> 1902 <211> 127 <212> PRT <213> Homo sapiens

<400> 1902 Met Tyr Phe Ser Ser Leu Phe Pro Tyr Val Val Leu Ala Cys Phe Leu 10 Val Arg Gly Leu Leu Leu Arg Gly Ala Val Asp Gly Ile Leu His Met 20 25 Phe Thr Pro Lys Leu Asp Lys Met Leu Asp Pro Gln Val Trp Arg Glu 35 40 45 Ala Ala Thr Gln Val Phe Ser Ala Leu Gly Leu Gly Phe Gly Gly Val 50 55 60 Ile Ala Phe Ser Ser Tyr Asn Lys Gln Asp Asn Asn Cys His Phe Asp 75 70 Ala Ala Leu Val Ser Phe Ile Asn Phe Phe Thr Ser Val Leu Ala Thr 85 90 Leu Val Val Phe Ala Val Leu Gly Phe Lys Ala Asn Ile Met Asn Glu 100 105 Lys Cys Val Val Glu Asn Ala Glu Lys Ile Leu Gly Tyr Arg Val 115 120

<210> 1903 <211> 83 <212> PRT <213> Homo sapiens

<400> 1903 Met Trp Lys Phe Val Ser Pro Leu Cys Met Ala Val Leu Thr Thr Ala 1 5 10 Ser Ile Ile Gln Leu Gly Val Thr Pro Pro Gly Tyr Ser Ala Trp Ile Lys Glu Glu Ala Ala Glu Arg Tyr Leu Tyr Phe Pro Asn Trp Ala Met 35 40 Ala Pro Leu Ile Thr Leu Ile Val Val Ala Thr Leu Pro Ile Pro Val 50 55 60 Val Phe Val Leu Arg His Phe His Leu Ile Cys Asp Gly Ser Asn Thr 65 75 70 Pro Cys Ile 83

<210> 1904 <211> 129 <212> PRT

<213> Homo sapiens

<400> 1904 Met Lys Met Phe Val Ala His Gly Phe Tyr Ala Ala Lys Phe Val Val 1 5 10 Ala Ile Gly Ser Val Ala Gly Leu Thr Val Ser Leu Leu Gly Ser Leu 25 Phe Pro Met Pro Arg Val Ile Tyr Ala Met Ala Gly Asp Gly Leu Leu 35 40 Phe Arg Phe Leu Ala His Val Ser Ser Tyr Thr Glu Thr Pro Val Val 55 Ala Cys Ile Val Ser Gly Phe Leu Ala Ala Leu Leu Ala Leu Leu Val 70 75 Ser Leu Arg Asp Leu Ile Glu Met Met Ser Ile Gly Thr Leu Leu Ala 85 90 Tyr Thr Leu Val Ser Val Cys Val Leu Leu Leu Arg His His Pro Glu 105 100 110 Ser Asp Ile Asp Gly Phe Val Lys Phe Leu Ser Glu Glu His Thr Cys 120 125 Ser 129

<210> 1905 <211> 93 <212> PRT <213> Homo sapiens

<400> 1905 Met Gly Leu Leu Met Met Ile Leu Gly Gln Ile Phe Leu Asn Gly Asn 1 5 10 15 Gln Ala Lys Glu Ala Glu Ile Trp Glu Met Leu Trp Arg Met Gly Val 20 25 Gln Arg Glu Arg Arg Leu Ser Ile Phe Gly Asn Pro Lys Arg Leu Leu 35 Ser Val Glu Phe Val Trp Gln Arg Tyr Leu Asp Tyr Arg Pro Val Thr 55 60 Asp Cys Lys Pro Val Glu Tyr Glu Phe Phe Trp Gly Pro Arg Ser His 70 75 Leu Glu Thr Thr Lys Met Lys Ile Leu Lys Phe Met Ala

<210> 1906 <211> 66 <212> PRT <213> Homo sapiens

35 40 45

Leu Ala Ser Gln His Ile Val Arg Thr Asp Leu His Val Gln Gly Pro
50 55 60

Cys Ile
65 66

<210> 1907 <211> 105 <212> PRT <213> Homo sapiens

<400> 1907

Met Leu Gln Leu Gly Pro Phe Leu Tyr Trp Thr Phe Leu Ala Ala Phe 1 5 10 Glu Gly Thr Val Phe Phe Gly Thr Tyr Phe Leu Phe Gln Thr Ala 20 25 Ser Leu Glu Glu Asn Gly Lys Val Tyr Gly Asn Trp Thr Phe Gly Thr 35 40 Ile Val Phe Thr Val Leu Val Phe Thr Val Thr Leu Lys Leu Ala Leu 60 Asp Thr Arg Phe Trp Thr Trp Ile Asn His Phe Val Ile Trp Gly Ser 70 75 Leu Ala Phe Tyr Val Phe Phe Ser Phe Phe Trp Gly Gly Ile Ile Trp 85 90 Pro Phe Leu Lys Gln Gln Arg Met Ala

<210> 1908 <211> 46 <212> PRT <213> Homo sapiens

<400> 1908
Met Gly Phe Leu Val Leu Lys Gln Pro Met Leu Val Ala Lys Val Phe

1 5 10 15 Pro Thr Leu Ala Gly Val Glu Ile Ile Leu Phe Thr Leu Lys Gly Phe 20 25 30

Pro Ile Leu Gly Ile Pro Val Gln Leu Pro Pro Thr Val \* 35 40

<210> 1909 <211> 139 <212> PRT <213> Homo sapiens

Asp Asp Arg Trp Ile Asn Asp Val Glu Asp Ser Tyr Gly Gln Gln Trp 40 Thr Tyr Glu Gln Arg Lys Ile Val Glu Phe Thr Cys His Thr Ala Phe 55 60 Phe Val Ser Ile Val Gly Val Gln Trp Ala Asp Leu Val Ile Cys Lys 70 75 Thr Arg Arg Asn Ser Val Phe Gln Pro Gly Met Lys Asn Lys Ile Leu 85 90 Ile Phe Gly Leu Phe Glu Glu Thr Ala Leu Ala Ala Phe Leu Ser Tyr 105 Cys Pro Gly Met Gly Val Ala Leu Lys Met Tyr Pro Leu Lys Pro Thr 120 Trp Arg Val Cys Ala Phe Pro Tyr Ser Leu Leu 135 139

<210> 1910 <211> 104 <212> PRT

<213> Homo sapiens

<400> 1910 Met Glu Gly Trp Phe Ala Val Leu Ser Thr Ala Asn Asp Val Leu Gly 10 Ala Pro Trp Asn Trp Leu Tyr Phe Ile Pro Leu Leu Ile Ile Gly Ala 20 25 Phe Phe Val Pro Thr Leu Val Leu Gly Val Leu Ser Gly Asp Phe Ala 40 3.5 45 Lys Glu Arg Glu Arg Val Glu Thr Arg Arg Ala Phe Met Lys Leu Arg 55 60 Arg Gln Gln Gln Ile Glu Arg Glu Leu Asn Gly Tyr Arg Val Trp Ile 70 75 Ala Lys Ala Glu Glu Val Met Leu Ala Glu Glu Asn Leu Tyr Pro Ser 85 His Ala Arg Pro Val Asn Pro \* 100 103

<210> 1911 <211> 116 <212> PRT <213> Homo sapiens

<400> 1911 Met Ala Val Ala Val Leu Leu Cys Gly Cys Ile Val Ala Thr Val Ser 5 10 Phe Phe Trp Glu Glu Ser Leu Thr Gln His Val Ala Gly Leu Leu Phe Leu Met Thr Gly Ile Phe Cys Thr Ile Ser Leu Cys Thr Tyr Ala Ala 40 Ser Ile Ser Tyr Asp Leu Asn Arg Leu Pro Lys Leu Ile Tyr Ser Leu 55 60 Pro Ala Asp Val Glu His Gly Tyr Ser Trp Ser Ile Phe Cys Ala Trp 70 75 Cys Ser Leu Gly Phe Ile Val Ala Ala Gly Gly Leu Cys Ile Ala Tyr

<210> 1912 <211> 105 <212> PRT <213> Homo sapiens

<210> 1913 <211> 141 <212> PRT <213> Homo sapiens

<400> 1913 Met Leu Val Tyr Val Trp Ser Arg Arg Ser Pro Arg Val Arg Val Asn 1 5 10 15 Phe Phe Gly Leu Leu Thr Phe Gln Ala Pro Phe Leu Pro Trp Ala Leu 20 25 30 25 Met Gly Phe Ser Leu Leu Gly Asn Ser Ile Leu Val Asp Leu Leu 3.5 40 45 Gly Ile Ala Val Gly His Ile Tyr Tyr Phe Leu Glu Asp Val Phe Pro 55 60 Asn Gln Pro Gly Arg Gln Glu Ala Pro Ala Asp Pro Trp Ala Phe Leu 70 75 Lys Leu Leu Gly Cys Pro Cys Arg Arg Pro Gln Leu Thr Cys Pro 85 90 95 Ser Leu Arg Asn Ser Gln Asp Pro Ile Cys His Pro Arg Ser Ser Asp 100 105 Pro His Pro Gly Ala Arg Pro Lys Arg Leu Leu Ala Ala Ser Ile Leu 115 120 125 Pro Met Thr Pro Thr Trp Gly Arg Lys Asn Pro Ser \* 135

<210> 1914 <211> 556 <212> PRT <213> Homo sapiens

<400> 1914 Met Lys Lys Val Leu Leu Leu Trp Lys Thr Val Leu Cys Thr Leu 10 Gly Gly Phe Glu Glu Leu Gln Ser Met Lys Ala Glu Lys Arg Ser Ile 2.0 Leu Gly Leu Pro Pro Leu Pro Glu Asp Ser Ile Lys Val Ile Arg Asn 3.5 Met Arg Ala Ala Ser Pro Pro Ala Ser Ala Ser Asp Leu Ile Glu Gln 55 60 Gln Gln Lys Arg Gly Arg Glu His Lys Ala Leu Ile Lys Gln Asp 70 75 Asn Leu Asp Ala Phe Asn Glu Arg Asp Pro Tyr Lys Ala Asp Asp Ser 85 90 Arg Glu Glu Glu Glu Asn Asp Asp Asp Asn Ser Leu Glu Gly Glu 100 105 110 Thr Phe Pro Leu Glu Arg Asp Glu Val Met Pro Pro Pro Leu Gln His 120 125 Pro Gln Thr Asp Arg Leu Thr Cys Pro Lys Gly Leu Pro Trp Ala Pro 135 140 Lys Val Arg Glu Lys Asp Ile Glu Met Phe Leu Glu Ser Ser Arg Ser 150 155 Lys Phe Ile Gly Tyr Thr Leu Gly Ser Asp Thr Asn Thr Val Val Gly 165 170 Leu Pro Arg Pro Ile His Glu Ser Ile Lys Thr Leu Lys Gln His Lys 185 Tyr Thr Ser Ile Ala Glu Val Gln Ala Gln Met Glu Glu Glu Tyr Leu 200 Arg Ser Pro Leu Ser Gly Gly Glu Glu Glu Val Glu Gln Val Pro Ala 215 220 Glu Thr Leu Tyr Gln Gly Leu Leu Pro Ser Leu Pro Gln Tyr Met Ile 230 235 Ala Leu Leu Lys Ile Leu Leu Ala Ala Ala Pro Thr Ser Lys Ala Lys 245 250 Thr Asp Ser Ile Asn Ile Leu Ala Asp Val Leu Pro Glu Glu Met Pro 260 265 270 Thr Thr Val Leu Gln Ser Met Lys Leu Gly Val Asp Val Asn Arg His 275 280 Lys Glu Val Ile Val Lys Ala Ile Ser Ala Val Leu Leu Leu Leu 295 300 Lys His Phe Lys Leu Asn His Val Tyr Gln Phe Glu Tyr Met Ala Gln 310 315 His Leu Val Phe Ala Asn Cys Ile Pro Leu Ile Leu Lys Phe Phe Asn 330 325 Gln Asn Ile Met Ser Tyr Ile Thr Ala Lys Asn Ser Ile Ser Val Leu 345 Asp Tyr Pro His Cys Val Val His Glu Leu Pro Glu Leu Thr Ala Glu 355 360 365 Ser Leu Glu Ala Gly Asp Ser Asn Gln Phe Cys Trp Arg Asn Leu Phe 375 380 Ser Cys Ile Asn Leu Leu Arg Ile Leu Asn Lys Leu Thr Lys Trp Lys 390 395 His Ser Arg Thr Met Met Leu Val Val Phe Lys Ser Ala Pro Ile Leu

```
405
                              410
Lys Arg Ala Leu Lys Val Lys Gln Ala Met Met Gln Leu Tyr Val Leu
       420
                     425
                                   430
Lys Leu Leu Lys Val Gln Thr Lys Tyr Leu Gly Arg Gln Trp Arg Lys
                       440
                                        445
Ser Asn Met Lys Thr Met Ser Ala Ile Tyr Gln Lys Val Arg His Arg
           455
Leu Asn Asp Asp Trp Ala Tyr Gly Asn Asp Leu Asp Ala Arg Pro Trp
                470
                                475
Asp Phe Gln Ala Glu Glu Cys Ala Leu Arg Ala Asn Ile Glu Arg Phe
            485
                              490
Asn Ala Arg Arg Tyr Asp Arg Ala His Ser Asn Pro Asp Phe Leu Pro
                          505
                                   510
Val Asp Asn Cys Leu Gln Ser Val Leu Gly Gln Arg Val Asp Leu Pro
              520
                                       525
Glu Asp Phe Gln Met Asn Tyr Asp Leu Trp Leu Glu Arg Glu Val Phe
 530 535
Ser Lys Pro Ile Ser Trp Glu Glu Leu Leu Gln *
545 550
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<210> 1915 <211> 212 <212> PRT <213> Homo sapiens

<400> 1915 Met Phe Leu Val Ala Val Trp Trp Arg Phe Gly Ile Leu Ser Ile Cys Met Leu Cys Val Gly Leu Val Leu Gly Phe Leu Ile Ser Ser Val Thr 20 25 Phe Phe Thr Pro Leu Gly Asn Leu Lys Ile Phe His Asp Asp Gly Val 40 4.5 Phe Trp Val Thr Phe Ser Cys Ile Ala Ile Leu Ile Pro Val Val Phe 60 Met Gly Cys Leu Arg Ile Leu Asn Ile Leu Thr Cys Gly Val Ile Gly 75 Ser Tyr Ser Val Val Leu Ala Ile Asp Ser Tyr Trp Ser Thr Ser Leu 85 90 Ser Tyr Ile Thr Leu Asn Val Leu Lys Arg Ala Leu Asn Lys Asp Phe 105 100 His Arg Ala Phe Thr Asn Val Pro Phe Gln Thr Asn Asp Phe Ile Ile 115 120 125 Leu Ala Val Trp Gly Met Leu Ala Val Ser Gly Ile Thr Leu Gln Ile 135 140 Arg Arg Glu Arg Gly Arg Pro Phe Phe Pro Pro His Pro Tyr Lys Leu 150 155 Trp Lys Gln Glu Arg Glu Arg Arg Val Thr Asn Ile Leu Asp Pro Ser 165 170 175 Tyr His Ile Pro Pro Leu Arg Glu Arg Leu Tyr Gly Arg Leu Thr Gln 185 190 180 Ile Lys Gly Leu Phe Gln Lys Glu Gln Pro Ala Gly Glu Arg Thr Pro 195 200 205 Leu Leu Leu \* 210 211

<210> 1916 <211> 172 <212> PRT <213> Homo sapiens

<400> 1916 Met Cys Thr Pro Val Arg Val Ser Ile Val Cys Val Met Gly Ala Val 10 Gly Ala Val Trp Thr Ala Pro Leu Pro Leu Pro Trp Ala Pro Thr Pro 2.0 Ser Ile His Leu Arg Glu Glu Gly Ala Ala Phe Pro Phe Cys Gly Val 35 40 Cys Val Leu Arg Pro Arg Arg Ser Lys Trp Arg Ser Trp Asp Val Asn 55 60 Leu Gly Pro Arg Arg Gly Leu Leu Gly Cys Gly Pro Cys Pro Ser 70 75 Gly Lys Pro Arg Val His Leu Gln Arg Thr Arg Ser Gly Ala Gly Ala 8.5 90 Glu Ala Gly Gly Leu Pro Thr Arg Gly Ser Met Arg Gly Cys Pro Phe 100 105 110Leu Gly Ser Ser Ala Ala Lys Cys Ser Leu Leu Leu Arg Pro Pro Ser Arg Gly Glu Ala Ser Pro Trp Leu Pro Glu Phe Met Thr His Pro Val 130 135 140 His His Gln Gln Leu Ala Cys Gly Ser Gly Trp Leu Gly Thr Lys His 150 155 Pro Gly Gly Thr Cys Ala Leu Gly Ser Thr Met \* 165 170 171

<210> 1917 <211> 72 <212> PRT <213> Homo sapiens

Met Arg Trp Gly Phe Leu Glu Ile Leu Phe Leu Arg Ser Trp Phe 1 

His Ser Trp Ile Cys Leu Leu Pro Thr Pro Gln Leu Pro Pro Asn Gly -25 

Ala Ser Ala Gly Ser Gln Asp Glu Gly Ser Arg Arg Leu Ser Leu Ser Glu Val Arg Gly Leu Met Asn His Val Pro Asn Leu Cys Val Ala Phe -50 

Leu Ser Ile Val Ser Ile Ser -70 71

<210> 1918 <211> 88 <212> PRT <213> Homo sapiens

<400> 1918 Met Thr Ser Leu Met Phe Leu Trp Arg Ala Leu Leu Glu Thr Ile Ser 5 10 Thr Asn Met Thr Phe Ser Leu Pro Leu Ala Ala Val Val Arg Ala Trp 25 Met Lys Pro Thr Gly Ser Gly Met Phe Leu Tyr Gln Tyr Leu Pro Val 40 45 Val Lys Ser Ser Gln Ala Val Phe Pro Val Val Ile Glu Ile Ser Ser 55 60 Ile Ser Gly Ser Ile Leu Pro Lys Phe Pro Met Leu Ser Leu Met Ser 70 75 Leu His Thr Gly Ser Ile Ile \* 85 87

<210> 1919 <211> 54 <212> PRT <213> Homo sapiens

<400> 1919 Met Leu Gly Pro Phe Ser Ser Leu Phe Leu Leu Trp Ser Phe Thr 10 15 5 Arg Phe Cys Ile His Phe Tyr Leu Ala Pro Ser His His Cys Leu Thr 20 25 30 Ala Ala Leu Leu Pro Phe Ser Leu His Pro Leu Tyr Ser Ser Leu Ser 35 40 Leu Ser Arg Ser Gln \* 50 53

<210> 1920 <211> 114 <212> PRT <213> Homo sapiens

<400> 1920

Met His Pro Pro Leu Thr Pro Pro Thr Pro Leu Cys Leu Trp Leu Arg 10 Leu Leu Lys Ala Gln Ile Leu Ser Tyr Pro Val Pro Arg Phe Glu Thr 20 25 His Ser Leu Ile Ser Arg Cys Ser Gln Val Pro Pro Thr Phe Leu Trp 3.5 40 Asp Ile Lys Lys Gly Val Arg Gly Gln Arg Glu Pro Ser Gly Pro Leu 50 55 Leu Pro Tyr Thr Leu His Cys Pro Phe Ser Pro His Gln Asn Ala Gln 65 70 75 Arg Arg Cys Asp Asp Ala Thr Glu Asp Tyr Ala Thr Trp Ser Asn Arg 85 90 95 Ser Gly Gln His Asp Gln Leu Ser Arg Gly Cys Leu Leu Pro Phe Leu 105 Leu

<210> 1921 <211> 139 <212> PRT <213> Homo sapiens

<400> 1921 Met Val Tyr Leu Tyr Ile Tyr Leu Asp Leu Phe Gln Phe Leu Ile Thr 10 Val Leu Gln Gly Phe Leu Phe Val Phe Glu Met Glu Phe His Ser Cys 20 Arg Pro Gly Gln Ser Ala Met Met Gln Ser Gln Leu Ala Ala Thr Ser 35 40 45 Ala Ser Arg Val Gln Val Ile Leu Val Val Ser Ala Pro Gln Glu Ala 55 60 Gly Thr Thr Gly Ala Arg His His Val Gln Leu Ile Phe Val Phe Leu 70 75 Leu Glu Met Gly Phe Cys His Val Gly Gln Ala Gly Leu Glu Leu Leu 8.5 90 Asn Ser Gly Asp Pro Pro Thr Ser Ala Ser Gln Ser Ala Gly Ile Arg 100 105 110 Gly Val Asn His Cys Ala Pro Pro Ile Asn Ser Leu Leu Thr Phe Gln 120 Ser Phe Ile His Leu Glu Cys Ile Val Ile \* 135

<210> 1922 <211> 52 <212> PRT <213> Homo sapiens

<210> 1923 <211> 71 <212> PRT <213> Homo sapiens

35 40 45

Tyr Leu Leu Phe Phe Leu Trp Thr Phe Lys Leu Phe Ser Gly Phe Thr
50 55 60

Leu Lys Ile Ile Gln Gln \*
65 70

<210> 1924 <211> 187 <212> PRT <213> Homo sapiens

<400> 1924 Met Leu Phe Ile Gln Tyr Leu Leu Pro Cys Leu Leu Leu Ser Ala Glu 5 10 Leu Ser Gly Thr Phe Phe Leu Tyr Asn Thr Cys His Leu His Val Pro 25 Cys Cys His Ser Leu Val Pro Thr Gly Pro Pro Ser Leu Ser Ser His 40 Phe Gln Ser Arg Gly Leu Cys Ala Pro Cys Ala Ser Ile Ala Asp Ser 55 Gly Ile Ala Asp Ser Gly Gly Asn Asn Leu Asn Phe Val Gly Ala Gly 70 Gly Val Ala Ser Gly His Leu Leu Ser Pro Leu Leu Gly Pro Gln Ser 85 90 Ser Pro Cys Pro His Cys Pro Arg Gly Gly Arg Leu Pro Ser Gln Pro 100 105 110 Leu Pro Leu Cys Ser Ala Arg Ser Trp Ala Gln Glu Ala Leu Arg Leu 120 115 125 Pro Ser Ser Ala Gln Leu Cys Pro Cys His Pro Leu Pro Arg Gly Leu 140 130 135 Gly Pro Val Ser Pro Ser Gly Leu Leu Ala Asn Ile Ser Tyr Arg His 150 155 Asn Trp Leu Leu Gly Ser Trp Pro Gly Trp Leu Ile Trp Gly Gly Lys 165 170 Asn Arg Gly Gly Leu Asn Ser Phe Leu Ala \* 180 185 186

<210> 1925 <211> 50 <212> PRT <213> Homo sapiens

<210> 1926 <211> 47 <212> PRT <213> Homo sapiens

<400> 1926

Met Gly Arg Tyr Arg Cys Ala Ser Leu Leu Phe Cys Phe Leu Leu Leu 1 15 Phe Phe Phe Phe Phe Trp Leu Trp Val Arg Asp Ile Phe Lys Leu Ala Gln 20 25 30 Lys Gly Arg Gly Trp Ser Leu Asp Pro His Val Ser Ile Thr \* 45 46

<210> 1927 <211> 149 <212> PRT <213> Homo sapiens

<400> 1927 Met Ala Thr Gly Leu Leu Ala Phe Leu Gly Leu Ala Ala Gly Gly Gln 10 Thr Leu Cys Pro Ala Gly Glu Leu Pro Gly His Ala Arg Ala Gln Ala 20 25 Ser Gly Ala Pro Gly Ser Val Leu Ile Ala Val Pro Gly Arg Arg Arg 35 40 35 4.5 Val His Thr Cys Gly Pro Gly Pro Ala Ala Pro Ser Thr Arg Gly Glu 50 60 Cys Pro Pro Pro Ala Leu Gly His Thr Arg Pro Ala Arg Pro Arg Pro 70 75 Val Leu Leu Arg Pro Ser Cys Ser Pro Gly Ala Arg Gly Ala Gly Thr 90 Trp Cys Cys Ala Pro Ala Thr Gly His Ser Ala Pro Arg Gly Cys Pro 100 105 110 Pro Ala Arg Ala Ala Pro Thr Gly Ser Ala Thr Pro Ala Pro Pro Pro 115 120 125 Ala Ala Cys Ala Ala Phe His Ser Ala Trp Ser Val Pro Pro Ala Gly 130 135 140 Arg Gln Gln Gly \* 145 148

<210> 1928 <211> 446 <212> PRT <213> Homo sapiens

<400> 1928

Met Ser Leu Trp Asn Gln Leu Val Val Pro Val Leu Phe Met Val Phe 1 5 10 15 Trp Leu Val Leu Phe Ala Leu Gln Ile Tyr Ser Tyr Phe Ser Thr Arg 20 25 30 Asp Gln Pro Ala Ser Arg Glu Arg Leu Leu Phe Leu Phe Leu Thr Ser

```
35
                        40
                                         45
Ile Ala Glu Cys Cys Ser Thr Pro Tyr Ser Leu Leu Gly Leu Val Phe
                    55
Thr Val Ser Phe Val Ala Leu Gly Val Leu Thr Leu Cys Lys Phe Tyr
                70
                                  75
Leu Gln Gly Tyr Arg Ala Phe Met Asn Asp Pro Ala Met Asn Arg Gly
              85
                               90
Met Thr Glu Gly Val Thr Leu Leu Ile Leu Ala Val Gln Thr Gly Leu
         100
                    105
                                   110
Ile Glu Leu Gln Val Val His Arg Ala Phe Leu Leu Ser Ile Ile Leu
              120
                               125
    115
Phe Ile Val Val Ala Ser Ile Leu Gln Ser Met Leu Glu Ile Ala Asp
 130 135
                            140
Pro Ile Val Leu Ala Leu Gly Ala Ser Arg Asp Lys Ser Leu Trp Lys
                150
                                155
His Phe Arg Ala Val Ser Leu Cys Leu Phe Leu Leu Val Phe Pro Ala
             165
                             170
Tyr Met Ala Tyr Met Ile Cys Gln Phe Phe His Met Asp Phe Trp Leu
         180
                 185
                                           190
Leu Ile Ile Ser Ser Ser Ile Leu Thr Ser Leu Gln Val Leu Gly
 195
           200
                               205
Thr Leu Phe Ile Tyr Val Leu Phe Met Val Glu Phe Arg Lys Glu
                 215
                            220
Pro Val Glu Asn Met Asp Asp Val Ile Tyr Tyr Val Asn Gly Thr Tyr
225 230
                                235
Arg Leu Leu Glu Phe Leu Val Ala Leu Cys Val Val Ala Tyr Gly Val
          245
                            250
                                               255
Ser Glu Thr Ile Phe Gly Glu Trp Thr Val Met Gly Ser Met Ile Ile
         260
                           265
Phe Ile His Ser Tyr Tyr Asn Val Trp Leu Arg Ala Gln Leu Gly Trp
                       280
Lys Ser Phe Leu Leu Arg Arg Asp Ala Val Asn Lys Ile Lys Ser Leu
                   295
                                    300
Pro Ile Ala Thr Lys Glu Gln Leu Glu Lys His Asn Asp Ile Cys Ala
              310
                                 315
Ile Cys Tyr Gln Asp Met Lys Ser Ala Val Ile Thr Pro Cys Ser His
           325 330
Phe Phe His Ala Gly Cys Leu Lys Lys Trp Leu Tyr Val Gln Glu Thr 340 345 350
                345
Cys Pro Leu Cys His Cys His Leu Lys Asn Ser Ser Gln Leu Pro Gly
                       360 . 365
Leu Gly Thr Glu Pro Val Leu Gln Pro His Ala Gly Ala Glu Gln Asn
                   375
                                    380
Val Met Phe Gln Glu Gly Thr Glu Pro Pro Gly Gln Glu His Thr Pro
                390
                                 395
Gly Thr Arg Ile Gln Glu Gly Ser Arg Asp Asn Asn Glu Tyr Ile Ala
                             410
Arg Arg Pro Asp Asn Gln Glu Gly Ala Phe Asp Pro Lys Glu Tyr Pro
                         425
His Ser Ala Lys Asp Glu Ala His Pro Val Glu Ser Ala *
                       440
                               . 445
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<210> 1929 <211> 120 <212> PRT

<213> Homo sapiens

<400> 1929 Met Val Leu Pro Leu Pro Trp Leu Ser Arg Tyr His Phe Leu Arg Leu 5 10 Leu Leu Pro Ser Trp Ser Leu Ala Pro Gln Gly Ser His Gly Cys Cys 20 25 Ser Gln Asn Pro Lys Ala Ser Met Glu Glu Gln Thr Asn Ser Arg Gly 35 40 Asn Gly Lys Met Thr Ser Pro Pro Arg Gly Pro Gly Thr His Arg Thr 55 Ala Glu Leu Ala Arg Ala Glu Glu Leu Leu Glu Gln Gln Leu Glu Leu 70 Tyr Gln Ala Leu Leu Glu Gly Gln Glu Gly Ala Trp Glu Ala Gln Ala 8.5 90 Leu Val Leu Lys Ile His Lys Leu Lys Glu Gln Met Arg Arg His Gln 100 105 Glu Ser Leu Gly Gly Gly Ala \* 119

<210> 1930 <211> 122 <212> PRT <213> Homo sapiens

<400> 1930 Met Thr Trp Leu Val Leu Leu Gly Thr Leu Leu Cys Met Leu Arg Val 1 5 10 Gly Leu Gly Thr Pro Asp Ser Glu Gly Phe Pro Pro Arg Ala Leu His 25 Asn Cys Pro Tyr Lys Cys Ile Cys Ala Ala Asp Leu Leu Ser Cys Thr 40 Gly Leu Gly Leu Gln Asp Val Pro Ala Glu Leu Pro Ala Gly Thr Ala 55 60 Asp Leu Asp Leu Ser His Asn Ala Leu Gln Arg Met Arg Pro Gly Trp 70 75 Leu Ala Pro Leu Phe Gln Leu Arg Ala Leu His Leu Asp His Asn Glu 85 90 Leu His Ala Leu Asp Arg Gly Val Phe Val Asn Ala Ser Gly Leu Arg 100 105 Leu Leu Asp Leu Ser Ser Asn Ala Glu Phe

120 122

<210> 1931 <211> 73 <212> PRT <213> Homo sapiens

115

<210> 1932 <211> 68 <212> PRT <213> Homo sapiens

<210> 1933 <211> 47 <212> PRT <213> Homo sapiens

<210> 1934 <211> 86 <212> PRT <213> Homo sapiens

Ala Val His Arg Lys Ala Gly Asp Thr Glu Val Gln Gln Ser Leu Leu 65 70 75 80
Leu Leu Leu Lys Lys \*

<210> 1935 <211> 76 <212> PRT <213> Homo sapiens

<400> 1935 Met Gly Glu Val Pro Lys Ala His Arg Leu Lys Leu Arg Trp Leu Phe 1 5 10 Pro Val Ser Leu Cys Arg Ala Pro Leu Leu Ser Thr Ala His Leu Ala 20 25 30 Leu Leu Pro Cys Cys Leu Leu Cys Ser Ser Cys Tyr Tyr Phe Pro 40 4.5 Phe Leu Ser Leu Leu Pro Pro Trp Pro Asn Leu Phe His Arg Asn Ile 55 Thr Gly Pro Ala Arg His Ser Gly Ser Pro Leu 70

<210> 1936 <211> 49 <212> PRT <213> Homo sapiens

<210> 1937 <211> 76 <212> PRT <213> Homo sapiens

50 55 60 Glu Ile Lys Phe Tyr Ile Gln Leu Ala Lys Lys Lys 65 70 75 76

<210> 1938 <211> 191 <212> PRT <213> Homo sapiens

<400> 1938 Met Ala Asp Glu Lys Thr Phe Arg Ile Gly Phe Ile Val Leu Gly Leu 1 10 Phe Leu Leu Ala Leu Gly Thr Phe Leu Met Ser His Asp Arg Pro Gln 25 3.0 Val Tyr Gly Thr Phe Tyr Ala Met Gly Ser Val Met Val Ile Gly Gly 35 40 45 Ile Ile Trp Ser Met Cys Gln Cys Tyr Pro Lys Ile Thr Phe Val Pro 55 Ala Asp Ser Asp Phe Gln Gly Ile Leu Ser Pro Lys Ala Met Gly Leu 70 Leu Glu Asn Gly Leu Ala Ala Glu Met Lys Ser Pro Ser Pro Gln Pro 85 90 Pro Tyr Val Arg Leu Trp Glu Glu Ala Ala Tyr Asp Gln Ser Leu Pro 100 105 Asp Phe Ser His Ile Gln Met Lys Val Met Ser Tyr Ser Glu Asp His 115 120 125 Arg Ser Leu Leu Ala Pro Glu Met Gly Gln Pro Lys Leu Gly Thr Ser 135 140 Asp Gly Gly Glu Gly Pro Gly Asp Val Gln Ala Trp Met Glu Ala 150 155 Ala Val Val Ile His Lys Gly Leu Asn Glu Ser Glu Gly Glu Arg Arg 165 170 175 Leu Thr Gln Ser Trp Pro Gly Pro Leu Ala Cys Pro Gln Gly Pro 185

<210> 1939 <211> 82 <212> PRT <213> Homo sapiens

<400> 1939 Met Val Arg Ser Ile Arg Leu Leu Phe Phe Phe Gly Trp Gly Phe Ser 5 10 Thr Thr Gln Gln Pro Ser Leu Cys Gln Asn Ser Leu Met Phe Pro Asp 2.0 25 Gly Ser Ser Phe Thr Pro Leu Ser Glu Ala Pro Lys Gly Ser Phe Pro 35 40 45 Gly Val Trp Thr Thr His Ser Ser Leu Ser Pro Asp Thr Pro Pro 55 Trp Val His Ser Ala Gly Trp Val Gln Thr Lys Trp Asn Pro Trp Asn 65 Leu \* 81

<210> 1940 <211> 101 <212> PRT <213> Homo sapiens

<210> 1941 <211> 88 <212> PRT <213> Homo sapiens

<400> 1941 Met Lys Ala Ser Val Leu Ser Pro Ser Phe Leu Leu Val Leu Trp Ser 1 5 10 Cys Phe Leu Ser Cys Ser Cys Met Glu Pro Gln Ser Gly Phe Pro Arg 20 25 Pro Ser Cys Phe Thr Val Gly Phe Leu Leu Arg Arg Arg Thr Lys Thr 35 40 Arg Arg Gln Lys Ala Thr Asn Thr Val Lys Met Arg Thr Thr Lys Ile 50 60Leu Lys Ile Lys Ile Asp Lys Arg Arg Trp Pro Thr Arg Met Ser Ser . 75 70 Lys Trp Asn Pro Lys Glu Trp 85 87

<210> 1942 <211> 46 <212> PRT <213> Homo sapiens

<210> 1943 <211> 155 <212> PRT <213> Homo sapiens

<400> 1943 Met Phe Thr Leu Leu Val Leu Leu Ser Gln Leu Pro Thr Val Thr Leu 1 5 10 Gly Phe Pro His Cys Ala Arg Gly Pro Lys Ala Ser Lys His Ala Gly 20 25 Glu Glu Val Phe Thr Ser Lys Glu Glu Ala Asn Phe Phe Ile His Arg Arg Leu Leu Tyr Asn Arg Phe Asp Leu Glu Leu Phe Thr Pro Gly Asn 55 60 Leu Glu Arg Glu Cys Asn Glu Glu Leu Cys Asn Tyr Glu Glu Ala Arg 70 75 Glu Ile Phe Val Asp Glu Asp Lys Thr Ile Ala Phe Trp Gln Glu Tyr 85 90 95 Ser Ala Lys Gly Pro Thr Thr Lys Ser Asp Gly Asn Arg Glu Lys Ile 110 100 105 Asp Val Met Gly Leu Leu Thr Gly Leu Ile Ala Ala Gly Val Phe Leu 120 125 Val Ile Phe Gly Leu Leu Gly Tyr Tyr Leu Cys Ile Thr Lys Cys Asn 130 135 140 Arg Leu Gln His Pro Cys Ser Ser Ala Val Tyr

<210> 1944 <211> 61 <212> PRT <213> Homo sapiens

150

<210> 1945 <211> 79 <212> PRT <213> Homo sapiens

<210> 1946 <211> 72 <212> PRT <213> Homo sapiens

<210> 1947 <211> 56 <212> PRT <213> Homo sapiens

<210> 1948 <211> 48 <212> PRT <213> Homo sapiens

<400> 1948

Met Ser Leu Leu Pro Pro Leu Ala Leu Leu Leu Leu Ala Ala 1 5 10 Leu Val Ala Pro Ala Thr Ala Ala Thr Ala Tyr Arg Pro Asp Trp Asn 25 Arg Leu Ser Gly Leu Thr Arg Ala Arg Val Glu Thr Cys Gly Gly \*

<210> 1949 <211> 136 <212> PRT <213> Homo sapiens

<400> 1949

Met Leu Leu Ala Thr Leu Leu Leu Leu Leu Gly Gly Ala Leu Ala 10. His Pro Asp Arg Ile Ile Phe Pro Asn His Ala Cys Glu Asp Pro Pro 25 20 Ala Val Leu Leu Glu Val Gln Gly Thr Leu Gln Arg Pro Leu Val Arg 35 40 Asp Ser Arg Thr Ser Pro Ala Asn Cys Thr Trp Leu Ile Leu Gly Ser 55 Lys Glu Gln Thr Val Thr Ile Arg Phe Gln Lys Leu His Leu Ala Cys

70 Gly Ser Glu Arg Leu Thr Leu Arg Ser Pro Leu Gln Pro Leu Ile Ser 85 90 Leu Cys Glu Ala Pro Pro Ser Pro Leu Gln Leu Pro Gly Gly Asn Val 105 100 110

Thr Ile Thr Tyr Ser Tyr Ala Gly Ala Lys Arg Pro Gln Gly His Gly 115 120

Phe Phe Cys Phe Leu Lys Ala Lys 135 136

> <210> 1950 <211> 78 <212> PRT <213> Homo sapiens

<400> 1950

Met Trp Ile Tyr Phe Trp Thr Leu Asn Ser Val Pro Val Ile Tyr Met 5 10 15 Ser Thr Leu Met Ser Ile Pro His Tyr Phe Asp Tyr Cys Cys Phe Ile 20 25 5 3.0 Val Ser Asp Ile Met Leu Pro Glu Ile Thr Phe Ser Thr Phe Ile Leu 35 40 45 Leu Leu Met Val Ala Leu Ala Ile Arg Gly Pro Leu His Phe Arg Arg 55 60 His Phe Arg Ile Asn Leu Ser Ile Ala Thr Lys Asn Ala \*

70 · 75 77

<210> 1951

<211> 89 <212> PRT <213> Homo sapiens

88

<210> 1952 <211> 47 <212> PRT <213> Homo sapiens

8.5

<210> 1953 <211> 56 <212> PRT <213> Homo sapiens

1220 Homo Dapacino

<210> 1954 <211> 425 <212> PRT <213> Homo sapiens

<400> 1954 Met Thr Leu Arg Pro Gly Thr Met Arg Leu Ala Cys Met Phe Ser Ser Ile Leu Leu Phe Gly Ala Ala Gly Leu Leu Leu Phe Ile Ser Leu Gln Asp Pro Thr Glu Leu Ala Pro Gln Gln Val Pro Gly Ile Lys Phe Asn Ile Arg Pro Arg Gln Pro His His Asp Leu Pro Pro Gly Gly Ser Gln Asp Gly Asp Leu Lys Glu Pro Thr Glu Arg Val Thr Arg Asp Leu Ser Ser Gly Ala Pro Arg Gly Arg Asn Leu Pro Ala Pro Asp Gln Pro Gln Pro Pro Leu Gln Arg Gly Thr Arg Leu Arg Leu Arg Gln Arg Arg Arg Arg Leu Leu Ile Lys Lys Met Pro Ala Ala Ala Thr Ile Pro Ala Asn Ser Ser Asp Ala Pro Phe Ile Arg Pro Gly Pro Gly Thr Leu Asp Gly Arg Trp Val Ser Leu His Arg Ser Gln Gln Glu Arg Lys Arg Val Met Gln Glu Ala Cys Ala Lys Tyr Arg Ala Ser Ser Ser Arg Arg Ala Val Thr Pro Arg His Val Ser Arg Ile Phe Val Glu Asp Arg His Arg Val Leu Tyr Cys Glu Val Pro Lys Ala Gly Cys Ser Asn Trp Lys Arg Val Leu Met Val Leu Ala Gly Leu Ala Ser Ser Thr Ala Asp Ile Gln His Asn Thr Val His Tyr Gly Ser Ala Leu Lys Arg Leu Asp Thr Phe Asp Arg Gln Gly Ile Leu His Arg Leu Ser Thr Tyr Thr Lys Met Leu Phe Val Arg Glu Pro Phe Glu Arg Leu Val Ser Ala Phe Arg Asp Lys Phe Glu His Pro Asn Ser Tyr Tyr His Pro Val Phe Gly Lys Ala Ile Leu Ala Arg Tyr Arg Ala Asn Ala Ser Arg Glu Ala Leu Arg Thr Gly Ser Gly Val Arg Phe Pro Glu Phe Val Gln Tyr Leu Leu Asp Val His Arg Pro Val Gly Met Asp Ile His Trp Asp His Val Ser Arg Leu Cys Ser Pro Cys Leu Ile Asp Tyr Asp Phe Val Gly Lys Phe Glu Ser Met Glu Asp Asp Ala Asn Phe Phe Leu Ser Leu Ile Arg Ala Pro Arg Asn Leu 355 360 Thr Phe Pro Arg Phe Lys Asp Arg His Ser Gln Glu Ala Arg Thr Thr . 380 Ala Arg Ile Ala His Gln Tyr Phe Ala Gln Leu Ser Ala Leu Gln Arg 395 400 Gln Arg Thr Tyr Asp Phe Tyr Tyr Met Asp Tyr Leu Met Phe Asn Tyr Ser Lys Pro Phe Ala Asp Leu Tyr \* 

<210> 1955 <211> 106 <212> PRT <213> Homo sapiens

<400> 1955 Met Val Cys Phe Leu Phe Ile Thr Pro Leu Ala Ala Ile Ser Gly Trp 10 Leu Cys Leu Arg Gly Ala Gln Asp His Leu Arg Leu His Ser Gln Leu 25 Glu Ala Val Gly Leu Ile Ala Leu Thr Ile Ala Leu Phe Thr Ile Tyr 45 40 Val Leu Trp Thr Leu Val Ser Phe Arg Tyr His Cys Gln Leu Tyr Ser 50 55 . 60 Glu Trp Arg Lys Thr Asn Gln Lys Val Arg Leu Lys Ile Arg Glu Ala 70 75 Asp Ser Pro Glu Gly Pro Gln His Ser Pro Leu Ala Ala Gly Leu Leu 85 90 Lys Lys Val Ala Glu Glu Thr Pro Val 100

<210> 1956 <211> 139 <212> PRT <213> Homo sapiens

<400> 1956 Met Val Leu Pro Phe Ile Cys Asn Leu Leu Arg Arg His Pro Ala Cys 1 5 10 15 Arg Val Leu Val His Arg Pro His Gly Pro Glu Leu Asp Ala Asp Pro 25 Tyr Asp Pro Gly Glu Glu Asp Pro Ala Gln Ser Arg Ala Leu Glu Ser Ser Leu Trp Glu Leu Gln Ala Leú Gln Arg His Tyr His Pro Glu Val 55 60 Ser Lys Ala Ala Ser Val Ile Asn Gln Ala Leu Ser Met Pro Glu Val 75 70 Ser Ile Ala Pro Leu Leu Glu Leu Thr Ala Tyr Glu Ile Phe Glu Arg 85 90 Asp Leu Lys Lys Gly Pro Glu Pro Val Pro Thr Gly Val Leu Ser 100 105 110 Gln Pro Arg Ala Cys Trp Asp Gly Arg Val Lys Leu Cys Ala Gln His 115 120 Phe His Ala Gln Leu Thr Leu Ala His Leu \* 135 138

<210> 1957 <211> 87 <212> PRT <213> Homo sapiens

<210> 1958 <211> 48 <212> PRT <213> Homo sapiens

<210> 1959 <211> 65 <212> PRT <213> Homo sapiens

<210> 1960 <211> 78 <212> PRT <213> Homo sapiens

<400> 1960

Met Ser Tyr Val Arg His Val Leu Ser Cys Leu Gly Gly Leu Ala 10 Leu Trp Arg Ala Gly Gln Trp Leu Trp Ala Gln Arg Leu Gly His Cys 25 30 His Thr Tyr Trp Ala Val Ser Glu Glu Leu Leu Pro Asn Ser Gly His 40 45 Gly Pro Asp Gly Glu Val Pro Lys Asp Lys Glu Gly Gly Val Phe Asp 55 60 Leu Gly Pro Phe Ile Val Gly Phe Trp Gly Pro Gln Ile \* 70

<210> 1961 <211> 77 <212> PRT

<213> Homo sapiens

<400> 1961 Met Trp Tyr Gly Val Phe Leu Trp Ala Leu Val Ser Ser Leu Phe Phe 10 His Val Pro Ala Gly Leu Leu Ala Leu Phe Thr Leu Arg His His Lys 20 25 3.0 Tyr Gly Ala Ala Ile Ala Gly Val Tyr Arg Ala Ala Gly Lys Glu Met 40 45 Ile Pro Phe Glu Ala Leu Thr Leu Gly Thr Gly Gln Thr Phe Cys Val 55 60 Leu Val Val Ser Phe Leu Arg Ile Leu Ala Thr Leu 65 70 75 76

<210> 1962 <211> 65 <212> PRT <213> Homo sapiens

<400> 1962 Met Phe Ser Ala Val Phe Pro Ala Val Ser Cys Gln Ile Ser Leu Leu 5 1.0 Ser Thr Cys Asn Ser Leu Gln His Phe Pro Tyr Ala Gly Val Leu Cys 20 25 Phe Arg Pro Val Leu Cys Leu Cys Pro Gly Gln Asp Phe Cys Gly Asn 35 40 45 Val Arg Cys Gln Trp Arg Leu Leu Ala Gly Val Asp Val Ser Asp Val 55

<210> 1963 <211> 53 <212> PRT <213> Homo sapiens <221> misc\_feature

<222> (1)...(53)
<223> Xaa = any amino acid or nothing

<210> 1964 <211> 232 <212> PRT <213> Homo sapiens

<400> 1964 Met Pro Ser Val His Arg Leu Leu Gly Pro Gln Pro Val Pro Ser Arg 1 5 10 Arg Leu Arg Leu Ala Leu Ala Leu Leu Ser Leu Gln Val Val Val 25 Phe Phe Leu Val Val Leu Gly Gln Gly Arg Leu Leu Gln Pro Cys Arg 40 45 Gly Cys Leu Glu Leu Pro Gly Gly Pro Gly Glu Ala Glu Asp His Gly 55 60 Asp Leu Gly Gln Gly Trp Val Gly Leu Leu Gln Ala Leu Asp Pro Leu 65 70 75 80 Ser His Arg Arg Leu Val Met Ser Thr Arg His Ala His Gly Glu Asp 85 90 Arg Ala Phe Leu His Phe Ile Asp Val Lys Leu Val Val Val Pro Ala 100 105 110 Thr Pro His Ile Leu Gln Val Gln Leu His Arg Val Val Glu Val Pro 115 120 125 Leu Leu Arg Arg Leu Phe His Phe Pro Leu Leu Arg Gly Gln Gln Val 135 140 Ser Ser Glu Asp Val Val Ile His Thr Leu Val Ala Glu Pro Gln Gly 145 150 155 160 Glu Gly Ala Leu Asn Lys Asp Arg Pro Gly Trp Ile Val Ala Gly Gln 165 170 175 Gly Gly Leu Leu Ile Gly Thr Leu Asp Ser Trp Cys Gly Asp Ile His 180 185 Ala Leu Cys Pro Thr Met Trp Gly Trp Gly Gly Ser Ala Ala Pro Val 200 195 205 Glu Ser Leu Gly Lys Gly Thr Ser Gly Glu Gly Asp Gly Arg Arg Gln 210 215 Gly Gln Arg Thr Gly Pro Gly \* 230 231

<210> 1965 <211> 253 <212> PRT

## <213> Homo sapiens

<400> 1965 Met Gly Cys Ala Ile Ile Ala Gly Phe Leu His Tyr Leu Phe Leu Ala 10 Cys Phe Phe Trp Met Leu Val Glu Ala Val Ile Leu Phe Leu Met Val 20 25 Arg Asn Leu Lys Val Val Asn Tyr Phe Ser Ser Arg Asn Ile Lys Met 40 Leu His Ile Cys Ala Phe Gly Tyr Gly Leu Pro Met Leu Val Val Val 55 Ile Ser Ala Ser Val Gln Pro Gln Gly Tyr Gly Met His Asn Arg Cys 70 75 80 Trp Leu Asn Thr Glu Thr Gly Phe Ile Trp Ser Phe Leu Gly Pro Val 85 90 Cys Thr Val Ile Val Ile Asn Ser Leu Leu Leu Thr Trp Thr Leu Trp 100 105 Ile Leu Arg Gln Arg Leu Ser Ser Val Asn Ala Glu Val Ser Thr Leu 120 125 Lys Asp Thr Arg Leu Leu Thr Phe Lys Ala Phe Ala Gln Leu Phe Ile 135 140 Leu Gly Cys Ser Trp Val Leu Gly Ile Phe Gln Ile Gly Pro Val Ala 150 155 Gly Val Met Ala Tyr Leu Phe His His His Gln Gln Pro Ala Gly Gly 165 170 175 Leu His Leu Pro His Pro Leu Ser Ala Gln Arg Pro Gly Thr Arg Arg 180 185 190 Ile Gln Glu Val Asp His Trp Glu Asp Glu Ala Gln Leu Pro Val Pro 195 200 205 Asp Leu Lys Asp Leu Ala Val Leu His Ala Ile Arg Phe Gln Asp Gly 210 215 220 Leu Lys Ser Phe Leu Ala Phe Lys Tyr Ala Met Glu Pro Thr Val Gly 225 230 235 Gly Thr Ser Ser Phe Pro Cys Arg Glu Pro Tyr Pro \* 245 250 252

<210> 1966 <211> 649 <212> PRT <213> Homo sapiens

<400> 1966 Met Val Thr Cys Phe Ile Ile Gly Leu Leu Phe Pro Val Phe Ser Val Cys Tyr Leu Ile Ala Pro Lys Ser Pro Leu Gly Leu Phe Ile Arg Lys 25 Pro Phe Ile Lys Phe Ile Cys His Thr Ala Ser Tyr Leu Thr Phe Leu 40 45 Phe Leu Leu Leu Ala Ser Gln His Ile Asp Arg Ser Asp Leu Asn 55 60 Arg Gln Gly Pro Pro Pro Thr Ile Val Glu Trp Met Ile Leu Pro Trp 70 75 Val Leu Gly Phe Ile Trp Gly Glu Ile Lys Gln Met Trp Asp Gly Gly 85 90 Leu Gln Asp Tyr Ile His Asp Trp Trp Asn Leu Met Asp Phe Val Met

			100					105					110		
Asn	Ser	Leu 115	Tyr	Leu	Ala	Thr	Ile 120		Leu	Lys	Ile	Val 125		Phe	Val
Lys	Tyr 130		Ala	Leu	Asn	Pro		Glu	Ser	Trp	Asp		Trp	His	Pro
Thr 145		Val	Ala	Glu	Ala 150		Phe	Ala	Ile	Ala 155		Ile	Phe	Ser	Ser 160
Leu	Arg	Leu	Ile	Ser 165		Phe	Thr	Ala	Asn 170		His	Leu	Gly	Pro 175	Leu
Gln	Ile	Ser	Leu 180	Gly	Arg	Met	Leu	Leu 185	Asp	Ile	Leu	Lys	Phe 190	Leu	Phe
		195	Leu				200					205			
Tyr	Phe 210	Tyr	Tyr	Glu	Glu	Thr 215	Lys	Gly	Leu	Thr	Суs 220	Lys	Gly	Ile	Arg
225		_	Gln		230					235					240
			Trp	245			_		250			_		255	
	_		Gln 260					265			-		270		
_		275	Asn	-			280					285			
	290		Asn			295					300				
305			Phe		310		_		_	315		-			320
			Leu	325					330					335	
	_	_	Leu 340		_	_		345				_	350	-	_
		355	Lys				360					365			
_	370		Arg Tyr	_		375		_			380		_		
385					390					395					400
			Glu	405					410					415	
			Glu 420			_		425	_	-		-	430		
		435	Ala				440					445		-	
_	450	-	Ser	_		455	_			-	460	-	-	-	
465	ser	ren	Phe	Asp	ьеи 470	unr	Thr	ьеи	TTE	475	Pro	Arg	ser	Ala	A1a 480
			Glu	485					490	_				495	
		•	Pro 500	_		_		505	_				510		_
_		515	Phe				520	_	-			525			
	530		Ala			535					540				
545			Ala	_	550			_		555					560
Gly	Leu	Ala	Ser	Arg 565	Gly	Asp	Leu	Ser	Ile 570	Pro	Gly	Leu	Ser	Glu 575	Gln

 Cys
 Val
 Leu
 Asp
 His
 Arg
 Glu
 Arg
 Asp
 Thr
 Asp
 Thr
 Leu
 Gly
 Leu
 Gly
 Leu
 Arg
 Val
 Ser
 Fro
 Phe
 Lys
 Ser
 Glu
 Lys
 Val
 Val
 Val
 Val
 Val
 Pro
 Phe
 Lys
 Glu
 Lys
 Lys</th

<210> 1967 <211> 80 <212> PRT <213> Homo sapiens

<210> 1968 <211> 49 <212> PRT <213> Homo sapiens

<210> 1969 <211> 150 <212> PRT <213> Homo sapiens

<400> 1969
Met His Val His Phe Trp Leu Val Thr Ala Ser Phe Ser Ser Val

10 Ala Trp Thr Thr Ala Glu Ile Thr Gly Gly Val Ser Gly Val Ala Ala
20 25 30 Gly Val Gly Ser Trp Glu Gly Gly Ser Glu Arg Gly Asp Arg Phe Gly Asp Phe Phe Thr Leu Asn Val Ser Val Phe Arg Gly Val Phe Phe Phe 55 60 Leu Ala Gly Leu Phe Ser Pro Ser Pro Ser Thr Pro Leu Ala Ser Ile 70 75 Ala Leu Ala Gly Ile Ser Lys Glu Ala Gly Asp Leu Glu Gly Glu Leu 85 90 Gly Val Leu Glu Asp Val Leu Lys Gly Ser Thr Asp Ser Ser Gln Val 100 105 110 Ser Gly Ser Lys Leu Tyr Asp Cys Trp Gly Ser Leu Gly Asp Ser Cys 115 120 125 Ile Phe Glu Val Glu Glu Lys Gly Leu Lys Leu Gly Ser Ser His Leu 130 135 Ser Ile Ser Lys Val \* 145 149

<210> 1970 <211> 48 <212> PRT <213> Homo sapiens

<210> 1971 <211> 64 <212> PRT <213> Homo sapiens

 <400> 1971

 Met Leu Ile Phe Phe Thr Val Leu Glu Leu Leu Leu Leu Ala Ala Tyr Ser Ser 1

 Val Phe Trp Trp Lys Gln Leu Tyr Ser Asn Asn Pro Gly Val Ser Met 20

 Leu Thr Cys Arg Leu Ile Pro Ala Val Ser Gln Val Gln Ala Thr Ile 35

 Ile Gln Pro Gln Lys Val Ala Lys Arg Arg Ile Asn Tyr Cys Ser \*

 56 \*\*

<210> 1972 <211> 211 <212> PRT

<213> Homo sapiens

<221> misc\_feature

<222> (1)...(211)

<223> Xaa = any amino acid or nothing

<400> 1972

Met Thr Arg Met Leu Asn Met Leu Ile Val Phe Arg Phe Leu Arg Ile 5 10 Ile Pro Ser Met Lys Pro Met Ala Val Val Ala Ser Thr Val Leu Gly 20 25 Leu Val Gln Asn Met Arg Ala Phe Gly Gly Ile Leu Val Val Val Tyr 35 40 Tyr Val Phe Ala Ile Ile Gly Ile Asn Leu Phe Arg Gly Val Ile Val 55 Ala Leu Pro Gly Asn Ser Ser Leu Ala Pro Ala Asn Gly Ser Ala Pro 75 Cys Gly Ser Phe Glu Gln Leu Glu Tyr Trp Ala Asn Asn Phe Asp Asp 85 90 Phe Xaa Ala Ala Leu Val Thr Leu Trp Asn Leu Met Val Val Asn Asn 105 110 100 Trp Gln Val Phe Leu Asp Ala Tyr Arg Arg Tyr Ser Gly Pro Trp Ser 115 120 125 Lys Ile Tyr Phe Val Leu Trp Trp Leu Val Ser Ser Val Ile Trp Val 140 135 Asn Leu Phe Leu Ala Leu Ile Leu Glu Asn Phe Leu His Lys Trp Asp 150 155 Pro Arg Ser His Leu Gln Pro Leu Ala Gly Thr Pro Glu Ala Thr Tyr 170 Gln Met Thr Val Glu Leu Leu Phe Arg Asp Ile Leu Glu Glu Pro Gly 180 185 Glu Asp Glu Leu Thr Glu Arg Leu Ser Gln His Pro His Leu Trp Leu 200

<210> 1973 <211> 53 <212> PRT

<213> Homo sapiens

<400> 1973

Cys Arg \* 210

<210> 1974 <211> 50

<212> PRT <213> Homo sapiens

<210> 1975 <211> 87 <212> PRT <213> Homo sapiens

<400> 1975 Met Cys Ser Ser Pro Ala Val Leu Leu Cys Ala Leu Val Val Gly Cys 5 10 Pro Val Gly Phe Pro His Glu Ala Asp Pro Gly Ser Met Gln Arg Ala 25 Ser Ser Leu Gly Leu His Gln Ala Ser Val Val Ser Ala Gly Trp Leu 40 45 35 Gly Gln Ala Arg His Gly Ala His Leu Gly Cys Ser Leu Leu Pro Ser 55 60 Gly Val His Gly Leu Trp Arg Pro Ser Val Gln Pro Arg Arg Asp Pro 70 Val Thr Glu Leu Gln Cys 85 86

<210> 1976 <211> 107 <212> PRT <213> Homo sapiens

<400> 1976 Met Ala Leu Tyr Glu Leu Phe Ser His Pro Val Glu Arg Ser Tyr Arg 1 5 10 15 Ala Gly Leu Cys Ser Lys Ala Ala Leu Phe Leu Leu Leu Ala Ala Ala 20 25 30 Leu Thr Tyr Ile Pro Pro Leu Leu Val Ala Phe Arg Ser His Gly Phe 40 45 Trp Leu Lys Arg Ser Ser Tyr Glu Glu Gln Pro Thr Val Arg Phe Gln 55 His Gln Val Leu Leu Val Ala Leu Leu Gly Pro Glu Ser Asp Gly Phe 70 75 65 Leu Ala Trp Ser Thr Phe Pro Ala Phe Asn Arg Gln Gln Gly Asp Arg 85 90 Leu Arg Val Pro Leu Val Ser Trp Arg Arg 100 105 106

<210> 1977 <211> 134 <212> PRT <213> Homo sapiens

<400> 1977 Met Val Thr Val Ala Met Ala Cys Ser Gly Ala Leu Thr Ala Leu Cys 1 •5 10 Cys Leu Phe Val Ala Met Gly Val Leu Arg Val Pro Trp His Cys Pro 25 2.0 3.0 Leu Leu Val Thr Glu Gly Leu Leu Asp Met Leu Ile Ala Gly Gly 35 40 Tyr Ile Pro Ala Leu Tyr Phe Tyr Phe His Tyr Leu Ser Ala Ala Tyr 50 55 60 Gly Ser Pro Val Cys Lys Glu Arg Gln Ala Leu Tyr Gln Ser Lys Gly 70 Tyr Ser Gly Phe Gly Cys Ser Phe His Gly Ala Asp Ile Gly Ala Gly 85 90 Ile Phe Ala Ala Leu Gly Ile Val Val Phe Ala Leu Gly Ala Val Leu 100 105 110 Ala Ile Lys Gly Tyr Arg Lys Val Arg Lys Leu Lys Glu Lys Pro Ala 120 1.15 Glu Met Phe Glu Phe \* 130 133

<210> 1978 <211> 61 <212> PRT <213> Homo sapiens

<210> 1979 <211> 66 <212> PRT <213> Homo sapiens

 $<\!\!400\!\!> 1979$  Met Leu Thr Ala Leu Pro Lys Ser Phe Val Phe Lys Val Val Gly Glu 1  $\cdot$  5  $\cdot$  10  $\cdot$  15 Trp Trp Leu Phe Ile Cys Leu Val Leu Ala Phe Ala Asp Gly Lys

```
20 25 30

Arg His Lys Tyr Ser Tyr Asp Ala Asn Val Phe Leu Gln Val Asn Tyr
35 40 45

Ile Thr Trp Pro Asp Ser Phe Ser Pro Val Pro Ser Leu Pro Pro Ile
50 55 60

Leu *
65
```

<210> 1980 <211> 51 <212> PRT <213> Homo sapiens

<210> 1981 <211> 79 <212> PRT <213> Homo sapiens

<400> 1981

<210> 1982 <211> 156 <212> PRT <213> Homo sapiens

<400> 1982

Met His Asn Asn Tyr Thr Ala Leu Leu Gly Val Trp Ile Tyr Gly Phe 1 5 10 15 Phe Val Leu Met Leu Leu Val Leu Asp Leu Leu Tyr Tyr Ser Ala Met 20 25 30

Asn Tyr Asp Ile Cys Lys Val Tyr Leu Ala Arg Trp Gly Ile Gln Gly 40 Arg Trp Met Lys Gln Asp Pro Arg Arg Trp Gly Asn Pro Ala Arg Ala 55 60 Pro Arg Pro Gly Gln Arg Ala Pro Gln Pro Gln Pro Pro Pro Gly Pro 70 75 Leu Pro Gln Ala Pro Gln Ala Val His Thr Leu Arg Gly Asp Ala His 90 Ser Pro Pro Leu Met Thr Phe Gln Ser Ser Ser Ala Trp Glu Gly Ala 105 Ser Gln Gln Glu Ile Pro Glu Asn Glu Glu Thr Glu Lys Gly Asp 115 120 125 Asp Gln Ile Ser Ser Phe Leu Gly Val Thr Ser Asn Thr Lys Glu Ala 130 135 140 Ser Val Ile Gly Ile Gln Lys Thr Val Asp Val Leu 150

<210> 1983 <211> 63 <212> PRT <213> Homo sapiens

<400> 1983

<210> 1984 <211> 232 <212> PRT <213> Homo sapiens

<400> 1984 Met Phe His Arg Cys Gly Ile Met Ala Leu Val Ala Ala Tyr Leu Asn 10 Phe Val Ser Gln Met Ile Ala Val Pro Ala Phe Cys Gln His Val Ser 25 Lys Val Ile Glu Ile Arg Thr Met Glu Ala Pro Tyr Phe Leu Pro Glu 35 40 His Ile Phe Arg Asp Lys Cys Met Leu Pro Lys Ser Leu Glu Lys His 50 60Glu Lys Asp Leu Tyr Phe Leu Thr Asn Lys Ile Ala Glu Ser Leu Gly 70 Gly Lys Trp Asp Ile Val Leu Arg Asp Cys Gln Phe Arg Met Leu Pro 90 Gln Val Thr Asp Glu Asp Arg Leu Ser Arg Arg Lys Ser Ile Val Asp 105 110 Thr Val Ser Ile Gln Val Asp Ile Leu Ser Asn Asn Val Pro Ser Asp

115 120 125 Asp Val Val Ser Asn Thr Glu Glu Ile Thr Phe Glu Ala Leu Lys Lys 130 135 140 Ala Ile Asp Thr Ser Gly Met Glu Glu Glu Lys Glu Lys Arg Arg 155 160 150 Leu Val Ile Glu Lys Phe Gln Lys Ala Pro Phe Glu Glu Ile Ala Ala 165 170 175 Gln Cys Glu Ser Lys Ala Asn Leu Leu His Asp Arg Leu Ala Gln Ile 185 Leu Glu Leu Thr Ile Arg Pro Pro Pro Ser Pro Ser Gly Thr Leu Thr 195 200 205 Ile Thr Ser Gly His Ala Gln Tyr Gln Ser Val Pro Val Tyr Glu Met 210 215 220 Lys Phe Pro Asp Leu Cys Val Tyr 230 232

<210> 1985 <211> 141 <212> PRT <213> Homo sapiens

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115 120 125 Ser Ser Trp Asp Tyr Arg Cys Ala Thr Thr Pro Gly \* 130 135 140

<210> 1986 <211> 292 <212> PRT <213> Homo sapiens

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130 135 140 Ser Leu Pro Gly Pro Gly Phe Leu Ala Leu Gly Ser Ala Gln Ala Leu 145 150 155 Leu Ile Leu Leu Ile Ala Met Ala Val Phe Pro Leu Arg Ala Glu 165 170 Arg Ala Glu Ser Lys Leu Glu Ser Cys \* 180 185

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Thr His Trp Ala Val Cys Gly Cys Gly Phe Ile Ser Glu Lys Leu \* 65 70 75 79

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is Pro Asp Arg IIe IIe Phe Pro Asn His Ala Cys Glu Asp Pro Pro 20 25 30 Ala Val Leu Leu Glu Val Gln Glv Thr Leu Gln Arg Pro Leu Val Arg

Ala Val Leu Leu Glu Val Gln Gly Thr Leu Gln Arg Pro Leu Val Arg 35 40 45 Asp Ser Arg Thr Ser Pro Ala Asn Cys Thr Trp Leu Ile Leu Gly Ser

Asp Ser Arg Thr Ser Pro Ala Ash Cys Thr Trp Leu IIe Leu Gly Ser
50 55 60
Lys Glu Arg Thr Val Thr Ile Arg Phe Gln Lys Leu His Leu Ala Cys

65 70 75 80
Gly Ser Glu Arg Leu Thr Leu Arg Ser Pro Leu Gln Pro Leu Ile Ser

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Thr Ile Thr Tyr Ser Tyr Ala Gly Gly Gln Ser Thr His Gly Pro Gly
115 120 125

Leu Pro Ala Leu Leu Gln Ala Ser Pro Ser Pro Trp Cys Leu Cys Arg 130 135 140

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Cys Ile Cys 163

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 Glu
 Gly
 Pro
 Gln
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 Asp
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 Ala
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 Arg
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 Gln
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WO 01/54477 PCT/US01/02687

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 WO 01/54477 PCT/US01/02687

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Ala Arg Ala Gly Gly Ser Glu
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<210> 2016 <211> 64 <212> PRT <213> Homo sapiens

<210> 2017 <211> 58 <212> PRT <213> Homo sapiens

(213) Homo Baptella

<210> 2018 <211> 66 <212> PRT <213> Homo sapiens

 WO 01/54477 PCT/US01/02687

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# PATENT COOPERATION TREATY

# **PCT**

# DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT

(PCT Article 17(2)(a), Rule 13ter.1(c) and 39)

Applicant's or agent's file reference		Date of mailing (day/month/year)					
	IMPORTANT DECLARATION	- w 1131 0003					
21272-018		8 7 JUN 2001					
International application No.	International filing date (day/month/year)	(Earliest) Priority date (day/month/year)					
	Thing the (any) mount year y	(Landest) I Horky date (day/monthlyeur)					
PCT/US01/02687	25 January 2001 (25.01.2001)	25 January 2000 (25.01.2000)					
International Patent Classification (IPC)	or both national classification and IPC	25 341411 2000 (25.01.2000)					
IDC(7): C13D 31/06 and US C1 . 435/00	•						
IPC(7): C12P 21/06 and US C1.: 435/69.1  Applicant							
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HYSEQ, INC.							
integ, ave.							
This International Searching Authority he	reby declares, according to Article 17(2)(a), that application for the reasons indicated below.	uo international search report					
ł <u> </u>		1					
1. The subject matter of the inter	rnational application relates to:						
a. scientific theories.							
b. mathematical theorie	es	1					
c. plant varieties.		}					
d. animal varieties.							
	processes for the production of plants and animals	other then migraphic legical processes					
and the products of		, other than microbiological processes					
· — ·	ethods of doing business.						
	ethods of performing purely mental acts.	·					
l —							
l	ethods of playing games.						
. 🗂	ent of the human body by surgery or therapy.						
	ent of the animal body by surgery or therapy.	1					
k. diagnostic methods	practised on the human or animal body.						
l. mere presentations	of information.						
m. computer programs	for which this International Searching Authority	is not equipped to search prior art.					
	,						
	carts of the international application to comply wi	th prescribed requirements prevents a					
meaningful search from being	_	,					
the description	the claims	the drawings					
3. The failure of the nucleotide							
, <del>_</del>							
of the Administrative Instructions prevents a meaningful search from being carried out:							
the written form has not been furnished or does not comply with the standard.							
the computer readable form has not been furnished or does not comply with the standard.							
4. Further comments:							
Name and mailing address of the ISA/US  Authorized officer A MADRIA							
Commissioner of Patents and Trademarks							
Box PCT Westlerges D.C. 20031							
Washington, D.C. 20231							

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)



## CORRECTED VERSION

### (19) World Intellectual Property Organization International Bureau





### (43) International Publication Date 2 August 2001 (02.08.2001)

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			60/231,414	8 September 2000 (08.09.2000)	
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0/186,350	2 March 2000 (02.03,2000)	US			
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0/190,076				14 September 2000 (14.09.2000)	U
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	14 August 2000 (14.08.2000)	US	·		U
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/227,182	22 August 2000 (22.08.2000)			20 October 2000 (20.10.2000)	U
/226,681			•	20 October 2000 (20.10.2000)	U
/227,009			60/240,960	20 October 2000 (20.10.2000)	U
/228,924			60/241,809	20 October 2000 (20.10.2000)	U
			60/241,785	20 October 2000 (20.10.2000)	U
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	0/184,664 0/186,350 0/189,874 0/190,076 0/198,123 0/205,515 0/214,886 0/215,135 0/216,647 0/216,880 0/217,487 0/217,496 0/217,496 0/225,757 0/225,266 0/225,213 0/225,213 0/225,268 0/225,213 0/225,214 0/225,268 0/225,214 0/225,268 0/225,214 0/225,214 0/225,214 0/225,214 0/226,279 0/226,681 0/227,009	0/184,664       24 February 2000 (24.02.2000)         0/186,350       2 March 2000 (02.03.2000)         0/189,874       16 March 2000 (16.03.2000)         0/199,076       17 March 2000 (17.03.2000)         0/198,123       18 April 2000 (18.04.2000)         0/205,515       19 May 2000 (19.05.2000)         0/214,886       28 June 2000 (28.06.2000)         0/215,135       30 June 2000 (30.06.2000)         0/216,647       7 July 2000 (07.07.2000)         0/217,487       11 July 2000 (11.07.2000)         0/217,496       11 July 2000 (11.07.2000)         0/220,963       26 July 2000 (26.07.2000)         0/220,964       26 July 2000 (26.07.2000)         0/225,270       14 August 2000 (14.08.2000)         0/225,213       14 August 2000 (14.08.2000)         0/225,213       14 August 2000 (14.08.2000)         0/225,258       14 August 2000 (14.08.2000)         1/224,519       14 August 2000 (14.08.2000)         1/225,268       14 August 2000 (14.08.2000)         1/225,267       14 August 2000 (14.08.2000)         1/225,268       14 August 2000 (14.08.2000)         1/225,268       14 August 2000 (14.08.2000)         1/225,268       14 August 2000 (14.08.2000)         14 August 2000 (22.08.2000)	0/184,664         24 February 2000 (24,02,2000)         US           0/186,350         2 March 2000 (02.03,2000)         US           0/189,874         16 March 2000 (16.03,2000)         US           0/190,076         17 March 2000 (17,03,2000)         US           0/198,123         18 April 2000 (18.04,2000)         US           0/205,515         19 May 2000 (19.05,2000)         US           0/214,886         28 June 2000 (28.06,2000)         US           0/214,886         28 June 2000 (30.06,2000)         US           0/216,647         7 July 2000 (07.07,2000)         US           0/216,880         7 July 2000 (07.07,2000)         US           0/217,496         11 July 2000 (11.07,2000)         US           0/2218,290         14 July 2000 (14.07,2000)         US           0/220,963         26 July 2000 (26.07,2000)         US           0/220,964         26 July 2000 (14.08,2000)         US           0/225,757         14 August 2000 (14.08,2000)         US           0/225,266         14 August 2000 (14.08,2000)         US           0/225,213         14 August 2000 (14.08,2000)         US           0/225,759         14 August 2000 (14.08,2000)         US           0/225,266         14 August 2000 (14.08	0.7164,664   24 February 2000 (24.02.2000)   US   60/231,243	

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60/251,989	8 December 2000 (08.12.2000)	US
60/259,678	11 December 2000 (11.12.2000)	US
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#### POLYNUCLEOTIDES ENCODING HUMAN PROTEASE HOMOLOGS

The present application claims the benefit of U.S.

5 Provisional Application Number 60/171,566 which was filed on December 22, 1999 and is herein incorporated by reference in its entirety.

#### 1. INTRODUCTION

The present invention relates to the discovery,

identification, and characterization of novel human
polynucleotides encoding proteins sharing sequence similarity
with mammalian proteases. The invention encompasses the
described polynucleotides, host cell expression systems, the
encoded protein, fusion proteins, polypeptides and peptides,
antibodies to the encoded proteins and peptides, and
genetically engineered animals that either lack or over
express the disclosed sequences, antagonists and agonists of
the proteins, and other compounds that modulate the expression
or activity of the proteins encoded by the disclosed
polynucleotides that can be used for diagnosis, drug
screening, clinical trial monitoring and the treatment of
physiological disorders.

### 2. BACKGROUND OF THE INVENTION

Proteases cleave protein substrates as part of degradation, maturation, and secretory pathways within the body. Proteases have been associated with, *inter alia*, regulating development, modulating cellular processes, fertility, and infectious disease.

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### 3. SUMMARY OF THE INVENTION

The present invention relates to the discovery, identification, and characterization of nucleotides that encode novel human proteins, and the corresponding amino acid sequences of these proteins. The novel human proteins (NHPs) described for the first time herein share structural similarity with animal proteases, and particularly trypsin-like proteases such as oviductin.

The novel human nucleic acid (cDNA) sequences described herein, encode a proteins/open reading frames (ORFs) of 306, 302, and 164 amino acids in length (see SEQ ID NOS: 2, 4, and 6 respectively).

of the described NHPs, including small molecules, large molecules, mutant NHPs, or portions thereof that compete with native NHPs, NHP peptides, and NHP antibodies, as well as nucleotide sequences that can be used to inhibit the expression of the described NHPs (e.g., antisense and ribozyme molecules, and gene or regulatory sequence replacement constructs) or to enhance the expression of the described NHPs (e.g., expression constructs that place the described sequence under the control of a strong promoter system), and transgenic animals that express a NHP transgene, or "knock-outs" (which can be conditional) that do not express a functional NHP.

Further, the present invention also relates to processes for identifying compounds that modulate, i.e., act as agonists or antagonists, of NHP expression and/or NHP activity that utilize purified preparations of the described NHP and/or NHP product, or cells expressing the same. Such compounds can be used as therapeutic agents for the treatment of any of a wide variety of symptoms associated with biological disorders or imbalances.

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4. DESCRIPTION OF THE SEQUENCE LISTING AND FIGURES
The Sequence Listing provides the sequences of the NHP
ORFs encoding the described NHP amino acid sequences. SEQ ID
NO: 7 describes an NHP ORF with flanking sequences.

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5. DETAILED DESCRIPTION OF THE INVENTION

The NHPs, described for the first time herein, are novel proteins that are expressed in, inter alia, human cell lines, and human thymus, trachea, kidney, prostate, testis, thyroid, salivary gland, stomach, placenta, mammary gland, adipose, skin, esophagus, bladder, pericardium, and fetal kidney cells.

The described sequences were compiled from gene trapped cDNAs and clones isolated from a human kidney cDNA library (Edge Biosystems, Gaithersburg, MD). The present invention encompasses the nucleotides presented in the Sequence Listing, 5 host cells expressing such nucleotides, the expression products of such nucleotides, and: (a) nucleotides that encode mammalian homologs of the described sequences, including the specifically described NHPs, and the NHP products; (b) nucleotides that encode one or more portions of a NHP that 10 correspond to functional domains of the NHP, and the polypeptide products specified by such nucleotide sequences, including but not limited to the novel regions of any active domain(s); (c) isolated nucleotides that encode mutant versions, engineered or naturally occurring, of a described 15 NHP in which all or a part of at least one domain is deleted or altered, and the polypeptide products specified by such nucleotide sequences, including but not limited to soluble proteins and peptides in which all or a portion of the signal sequence is deleted; (d) nucleotides that encode chimeric 20 fusion proteins containing all or a portion of a coding region of a NHP, or one of its domains (e.g., a receptor or ligand binding domain, accessory protein/self-association domain, etc.) fused to another peptide or polypeptide; or (e) therapeutic or diagnostic derivatives of the described 25 polynucleotides such as oligonucleotides, antisense polynucleotides, ribozymes, dsRNA, or gene therapy constructs comprising a sequence first disclosed in the Sequence Listing. As discussed above, the present invention includes:

(a) the human DNA sequences presented in the Sequence Listing

(and vectors comprising the same) and additionally

contemplates any nucleotide sequence encoding a contiguous NHP

open reading frame (ORF), or a contiguous exon splice junction

first described in the Sequence Listing, that hybridizes to a

complement of a DNA sequence presented in the Sequence Listing

under highly stringent conditions, e.g., hybridization to

filter-bound DNA in 0.5 M NaHPO<sub>4</sub>, 7% sodium dodecyl sulfate

(SDS), 1 mM EDTA at 65°C, and washing in 0.1xSSC/0.1% SDS at

68°C (Ausubel F.M. et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3) and encodes a functionally equivalent gene product. Additionally 5 contemplated are any nucleotide sequences that hybridize to the complement of the DNA sequence that encode and express an amino acid sequence presented in the Sequence Listing under moderately stringent conditions, e.g., washing in  $0.2 \times SSC/0.1\%$ SDS at  $42\,^{\circ}\text{C}$  (Ausubel et al., 1989, supra), yet still encode a 10 functionally equivalent NHP product. Functional equivalents of a NHP include naturally occurring NHPs present in other species and mutant NHPs whether naturally occurring or engineered (by site directed mutagenesis, gene shuffling, directed evolution as described in, for example, U.S. Patent 15 No. 5,837,458). The invention also includes degenerate nucleic acid variants of the disclosed NHP polynucleotide sequences.

Additionally contemplated are polynucleotides encoding a NHP ORF, or its functional equivalent, encoded by a 20 polynucleotide sequence that is about 99, 95, 90, or about 85 percent similar or identical to corresponding regions of the nucleotide sequences of the Sequence Listing (as measured by BLAST sequence comparison analysis using, for example, the GCG sequence analysis package using standard default settings).

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The invention also includes nucleic acid molecules, preferably DNA molecules, that hybridize to, and are therefore the complements of, the described NHP nucleotide sequences. Such hybridization conditions may be highly stringent or less highly stringent, as described above. In instances where the 30 nucleic acid molecules are deoxyoligonucleotides ("DNA oligos"), such molecules are generally about 16 to about 100 bases long, or about 20 to about 80, or about 34 to about 45 bases long, or any variation or combination of sizes represented therein that incorporate a contiguous region of 35 sequence first disclosed in the Sequence Listing. oligonucleotides can be used in conjunction with the

polymerase chain reaction (PCR) to screen libraries, isolate clones, and prepare cloning and sequencing templates, etc.

Alternatively, such NHP oligonucleotides can be used as hybridization probes for screening libraries, and assessing 5 gene expression patterns (particularly using a micro array or high-throughput "chip" format). Additionally, a series of the described NHP oligonucleotide sequences, or the complements thereof, can be used to represent all or a portion of the described NHP sequences. An oligonucleotide or polynucleotide 10 sequence first disclosed in at least a portion of one or more of the sequences of SEQ ID NOS: 1-7 can be used as a hybridization probe in conjunction with a solid support matrix/substrate (resins, beads, membranes, plastics, polymers, metal or metallized substrates, crystalline or polycrystalline substrates, etc.). Of particular note are spatially addressable arrays (i.e., gene chips, microtiter plates, etc.) of oligonucleotides and polynucleotides, or corresponding oligopeptides and polypeptides, wherein at least one of the biopolymers present on the spatially addressable array comprises an oligonucleotide or polynucleotide sequence 20 first disclosed in at least one of the sequences of SEQ ID NOS: 1-7, or an amino acid sequence encoded thereby. Methods for attaching biopolymers to, or synthesizing biopolymers on, solid support matrices, and conducting binding studies thereon 25 are disclosed in, inter alia, U.S. Patent Nos. 5,700,637, 5,556,752, 5,744,305, 4,631,211, 5,445,934, 5,252,743, 4,713,326, 5,424,186, and 4,689,405 the disclosures of which are herein incorporated by reference in their entirety.

Addressable arrays comprising sequences first disclosed in SEQ ID NOS:1-7 can be used to identify and characterize the temporal and tissue specific expression of a sequence. These addressable arrays incorporate oligonucleotide sequences of sufficient length to confer the required specificity, yet be within the limitations of the production technology. The length of these probes is within a range of between about 8 to about 2000 nucleotides. Preferably the probes consist of 60

nucleotides and more preferably 25 nucleotides from the sequences first disclosed in SEQ ID NOS:1-7.

For example, a series of the described oligonucleotide sequences, or the complements thereof, can be used in chip 5 format to represent all or a portion of the described sequences. The oligonucleotides, typically between about 16 to about 40 (or any whole number within the stated range) nucleotides in length can partially overlap each other and/or the sequence may be represented using oligonucleotides that do 10 not overlap. Accordingly, the described polynucleotide sequences shall typically comprise at least about two or three distinct oligonucleotide sequences of at least about 8 nucleotides in length that are each first disclosed in the described Sequence Listing. Such oligonucleotide sequences 15 can begin at any nucleotide present within a sequence in the Sequence Listing and proceed in either a sense (5'-to-3') orientation vis-a-vis the described sequence or in an antisense orientation.

Microarray-based analysis allows the discovery of broad
20 patterns of genetic activity, providing new understanding of
gene functions and generating novel and unexpected insight
into transcriptional processes and biological mechanisms. The
use of addressable arrays comprising sequences first disclosed
in SEQ ID NOS:1-7 provides detailed information about
25 transcriptional changes involved in a specific pathway,
potentially leading to the identification of novel components
or gene functions that manifest themselves as novel
phenotypes.

Probes consisting of sequences first disclosed in SEQ ID NOS:1-7 can also be used in the identification, selection and validation of novel molecular targets for drug discovery. The use of these unique sequences permits the direct confirmation of drug targets and recognition of drug dependent changes in gene expression that are modulated through pathways distinct from the drugs intended target. These unique sequences therefore also have utility in defining and monitoring both drug action and toxicity.

As an example of utility, the sequences first disclosed in SEQ ID NOS:1-7 can be utilized in microarrays or other assay formats, to screen collections of genetic material from patients who have a particular medical condition. These investigations can also be carried out using the sequences first disclosed in SEQ ID NOS:1-7 in silico and by comparing previously collected genetic databases and the disclosed sequences using computer software known to those in the art.

Thus the sequences first disclosed in SEQ ID NOS:1-7 can
10 be used to identify mutations associated with a particular
disease and also as a diagnostic or prognostic assay.

Although the presently described sequences have been specifically described using nucleotide sequence, it should be appreciated that each of the sequences can uniquely be 15 described using any of a wide variety of additional structural attributes, or combinations thereof. For example, a given sequence can be described by the net composition of the nucleotides present within a given region of the sequence in conjunction with the presence of one or more specific 20 oligonucleotide sequence(s) first disclosed in the SEQ ID NOS: 1-7. Alternatively, a restriction map specifying the relative positions of restriction endonuclease digestion sites, or various palindromic or other specific oligonucleotide sequences can be used to structurally describe a given 25 sequence. Such restriction maps, which are typically generated by widely available computer programs (e.g., the University of Wisconsin GCG sequence analysis package, SEQUENCHER 3.0, Gene Codes Corp., Ann Arbor, MI, etc.), can optionally be used in conjunction with one or more discrete 30 nucleotide sequence(s) present in the sequence that can be described by the relative position of the sequence relative to one or more additional sequence(s) or one or more restriction sites present in the disclosed sequence.

For oligonucleotide probes, highly stringent conditions 35 may refer, e.g., to washing in 6xSSC/0.05% sodium pyrophosphate at 37°C (for 14-base oligos), 48°C (for 17-base oligos), 55°C (for 20-base oligos), and 60°C (for 23-base

oligos). These nucleic acid molecules may encode or act as NHP sequence antisense molecules, useful, for example, in NHP gene regulation (for and/or as antisense primers in amplification reactions of NHP gene nucleic acid sequences).

With respect to NHP gene regulation, such techniques can be used to regulate biological functions. Further, such sequences may be used as part of ribozyme and/or triple helix sequences that are also useful for NHP gene regulation.

Inhibitory antisense or double stranded oligonucleotides

10 can additionally comprise at least one modified base moiety
which is selected from the group including but not limited to
5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil,
hypoxanthine, xantine, 4-acetylcytosine,
5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl
15 2-thiouridine, 5-carboxymethylaminomethyluracil,
dihydrouracil, beta-D-galactosylqueosine, inosine,
N6-isopentenyladenine, 1-methylguanine, 1-methylinosine,

2,2-dimethylguanine, 2-methyladenine, 2-methylguanine,

3-methylcytosine, 5-methylcytosine, N6-adenine,

7-methylguanine, 5-methylaminomethyluracil,
5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine,
5'-methoxycarboxymethyluracil, 5-methoxyuracil,
2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid
(v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine,

5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

The antisense oligonucleotide can also comprise at least one modified sugar moiety selected from the group including but not limited to arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the antisense oligonucleotide will comprise at least one modified phosphate backbone

35 selected from the group consisting of a phosphorothioate, a phosphorodithioate, a phosphoramidate,

a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal or analog thereof.

In yet another embodiment, the antisense oligonucleotide is an α-anomeric oligonucleotide. An α-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641). The oligonucleotide is a 2'-0-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analogue (Inoue et al., 1987, FEBS Lett. 215:327-330). Alternatively, double stranded RNA can be used to disrupt the expression and function of a targeted NHP.

Oligonucleotides of the invention can be synthesized by standard methods known in the art, e.g. by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothicate oligonucleotides can be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), and methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. U.S.A. 85:7448-7451), etc.

Low stringency conditions are well known to those of skill in the art, and will vary predictably depending on the specific organisms from which the library and the labeled sequences are derived. For guidance regarding such conditions see, for example, Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual (and periodic updates thereof), Cold Springs Harbor Press, N.Y.; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y.

Alternatively, suitably labeled NHP nucleotide probes can be used to screen a human genomic library using appropriately stringent conditions or by PCR. The identification and characterization of human genomic clones is helpful for identifying polymorphisms (including, but not limited to, nucleotide repeats, microsatellite alleles, single nucleotide

polymorphisms, or coding single nucleotide polymorphisms), determining the genomic structure of a given locus/allele, and designing diagnostic tests. For example, sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (e.g., splice acceptor and/or donor sites), etc., that can be used in diagnostics and pharmacogenomics.

10 Further, a NHP homolog can be isolated from nucleic acid from an organism of interest by performing PCR using two degenerate or "wobble" oligonucleotide primer pools designed on the basis of amino acid sequences within the NHP products disclosed herein. The template for the reaction may be total RNA, mRNA, and/or cDNA obtained by reverse transcription of mRNA prepared from human or non-human cell lines or tissue known or suspected to express an allele of a NHP gene.

The PCR product can be subcloned and sequenced to ensure that the amplified sequences represent the sequence of the 20 desired NHP. The PCR fragment can then be used to isolate a full length cDNA clone by a variety of methods. For example, the amplified fragment can be labeled and used to screen a cDNA library, such as a bacteriophage cDNA library. Alternatively, the labeled fragment can be used to isolate genomic clones via the screening of a genomic library.

PCR technology can also be used to isolate full length cDNA sequences. For example, RNA can be isolated, following standard procedures, from an appropriate cellular or tissue source (i.e., one known, or suspected, to express a NHP gene, such as, for example, testis tissue). A reverse transcription (RT) reaction can be performed on the RNA using an oligonucleotide primer specific for the most 5' end of the amplified fragment for the priming of first strand synthesis. The resulting RNA/DNA hybrid may then be "tailed" using a standard terminal transferase reaction, the hybrid may be digested with RNase H, and second strand synthesis may then be primed with a complementary primer. Thus, cDNA sequences

upstream of the amplified fragment can be isolated. For a review of cloning strategies that can be used, see e.g., Sambrook et al., 1989, supra.

A cDNA encoding a mutant NHP gene can be isolated, for 5 example, by using PCR. In this case, the first cDNA strand may be synthesized by hybridizing an oligo-dT oligonucleotide to mRNA isolated from tissue known or suspected to be expressed in an individual putatively carrying a mutant NHP allele, and by extending the new strand with reverse 10 transcriptase. The second strand of the cDNA is then synthesized using an oligonucleotide that hybridizes specifically to the 5' end of the normal gene. Using these two primers, the product is then amplified via PCR, optionally cloned into a suitable vector, and subjected to DNA sequence 15 analysis through methods well known to those of skill in the art. By comparing the DNA sequence of the mutant NHP allele to that of a corresponding normal NHP allele, the mutation(s) responsible for the loss or alteration of function of the mutant NHP gene product can be ascertained.

20 Alternatively, a genomic library can be constructed using DNA obtained from an individual suspected of or known to carry a mutant NHP allele (e.g., a person manifesting a NHP-associated phenotype such as, for example, obesity, high blood pressure, connective tissue disorders, infertility, etc.), or a cDNA library can be constructed using RNA from a tissue known, or suspected, to express a mutant NHP allele. A normal NHP gene, or any suitable fragment thereof, can then be labeled and used as a probe to identify the corresponding mutant NHP allele in such libraries. Clones containing mutant NHP gene sequences can then be purified and subjected to sequence analysis according to methods well known to those skilled in the art.

Additionally, an expression library can be constructed utilizing cDNA synthesized from, for example, RNA isolated from a tissue known, or suspected, to express a mutant NHP allele in an individual suspected of or known to carry such a mutant allele. In this manner, gene products made by the

putatively mutant tissue can be expressed and screened using standard antibody screening techniques in conjunction with antibodies raised against normal NHP product, as described (For screening techniques, see, for example, Harlow, 5 E. and Lane, eds., 1988, "Antibodies: A Laboratory Manual", Cold Spring Harbor Press, Cold Spring Harbor.) Additionally, screening can be accomplished by screening with labeled NHP fusion proteins, such as, for example, alkaline phosphatase-NHP or NHP-alkaline phosphatase fusion proteins. 10 In cases where a NHP mutation results in an expressed gene product with altered function (e.g., as a result of a missense or a frameshift mutation), polyclonal antibodies to NHP are likely to cross-react with a corresponding mutant NHP gene product. Library clones detected via their reaction with such 15 labeled antibodies can be purified and subjected to sequence analysis according to methods well known in the art.

The invention also encompasses (a) DNA vectors that contain any of the foregoing NHP coding sequences and/or their complements (i.e., antisense); (b) DNA expression vectors that 20 contain any of the foregoing NHP coding sequences operatively associated with a regulatory element that directs the expression of the coding sequences (for example, baculo virus as described in U.S. Patent No. 5,869,336 herein incorporated by reference); (c) genetically engineered host cells that 25 contain any of the foregoing NHP coding sequences operatively associated with a regulatory element that directs the expression of the coding sequences in the host cell; and (d) genetically engineered host cells that express an endogenous NHP sequence under the control of an exogenously introduced 30 regulatory element (i.e., gene activation). As used herein, regulatory elements include, but are not limited to, inducible and non-inducible promoters, enhancers, operators and other elements known to those skilled in the art that drive and regulate expression. Such regulatory elements include but are 35 not limited to the human cytomegalovirus (hCMV) immediate early gene, regulatable, viral elements (particularly retroviral LTR promoters), the early or late promoters of SV40

adenovirus, the *lac* system, the *trp* system, the *TAC* system, the *TRC* system, the major operator and promoter regions of phage lambda, the control regions of fd coat protein, the promoter for 3-phosphoglycerate kinase (PGK), the promoters of acid phosphatase, and the promoters of the yeast  $\alpha$ -mating factors.

The present invention also encompasses antibodies and anti-idiotypic antibodies (including Fab fragments), antagonists and agonists of a NHP, as well as compounds or nucleotide constructs that inhibit expression of a NHP gene (transcription factor inhibitors, antisense and ribozyme molecules, or gene or regulatory sequence replacement constructs), or promote the expression of a NHP (e.g., expression constructs in which NHP coding sequences are operatively associated with expression control elements such as promoters, promoter/enhancers, etc.).

The NHPs or NHP peptides, NHP fusion proteins, NHP nucleotide sequences, antibodies, antagonists and agonists can be useful for the detection of mutant NHPs or inappropriately 20 expressed NHPs for the diagnosis of disease. The NHP proteins or peptides, NHP fusion proteins, NHP nucleotide sequences, host cell expression systems, antibodies, antagonists, agonists and genetically engineered cells and animals can be used for screening for drugs (or high throughput screening of 25 combinatorial libraries) effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of a NHP in the body. The use of engineered host cells and/or animals may offer an advantage in that such systems allow not only for the identification of compounds 30 that bind to the endogenous receptor for a NHP, but can also identify compounds that trigger NHP-mediated activities or pathways.

Finally, the NHP products can be used as therapeutics.

For example, soluble derivatives such as NHP peptides/domains

corresponding to NHP, NHP fusion protein products (especially NHP-Ig fusion proteins, i.e., fusions of a NHP, or a domain of a NHP, to an IgFc), NHP antibodies and anti-idiotypic

antibodies (including Fab fragments), antagonists or agonists (including compounds that modulate or act on downstream targets in a NHP-mediated pathway) can be used to directly treat diseases or disorders. For instance, the administration 5 of an effective amount of soluble NHP, or a NHP-IgFc fusion protein or an anti-idiotypic antibody (or its Fab) that mimics the NHP could activate or effectively antagonize the endogenous NHP receptor. Nucleotide constructs encoding such NHP products can be used to genetically engineer host cells to 10 express such products in vivo; these genetically engineered cells function as "bioreactors" in the body delivering a continuous supply of a NHP, a NHP peptide, or a NHP fusion protein to the body. Nucleotide constructs encoding functional NHP, mutant NHPs, as well as antisense and ribozyme 15 molecules can also be used in "gene therapy" approaches for the modulation of NHP expression. Thus, the invention also encompasses pharmaceutical formulations and methods for treating biological disorders.

Various aspects of the invention are described in greater 20 detail in the subsections below.

### 5.1 THE NHP SEQUENCES

The cDNA sequences (SEQ ID NO: 1, 3, and 5) and the corresponding deduced amino acid sequences of the described NHP are presented in the Sequence Listing. SEQ ID NO:7 describes a NHP ORF as well as flanking regions. The NHP nucleotides were obtained from human cDNA libraries using probes and/or primers generated from human gene trapped sequence tags. Expression analysis has provided evidence that the described NHP can be expressed a variety of human cells as well as gene trapped human cells. In addition, the described NHP sequences can contain a variety of polymorphisms such as at nucleotide 68 of SEQ ID NO:1 and nucleotide 56 of SEQ ID NO:3 which both can be a G or an A that can give rise to corresponding arg or gln at amino acid position 23 of SEQ ID NO:2, or residue 19 of SEQ ID NO:4. The described NHP sequences can also contain A-G polymorphisms at nucleotide 82

of SEQ ID NO:1 and nucleotide 70 of SEQ ID NO:3 which can give rise to a corresponding ala or thr at amino acid position 28 of SEQ ID NO:2, or residue 24 of SEQ ID NO:4. The described NHPs share similarity with trypsin-like proteases, plasminogen activators, and human plasma kallikrein precursor.

### 5.2 NHPs AND NHP POLYPEPTIDES

NHPs, polypeptides, peptide fragments, mutated, truncated, or deleted forms of the NHPs, and/or NHP fusion proteins can be prepared for a variety of uses. These uses include, but are not limited to, the generation of antibodies, as reagents in diagnostic assays, for the identification of other cellular gene products related to a NHP, as reagents in assays for screening for compounds that can be as pharmaceutical reagents useful in the therapeutic treatment of mental, biological, or medical disorders and disease.

The Sequence Listing discloses the amino acid sequence encoded by the described NHP polynucleotides. The NHPs display initiator methionines in DNA sequence contexts

20 consistent with a translation initiation site, and display a consensus signal sequence.

The NHP amino acid sequences of the invention include the amino acid sequences presented in the Sequence Listing as well as analogues and derivatives thereof, as well as any oligopeptide sequence of at least about 10-40, generally about 12-35, or about 16-30 amino acids in length first disclosed in the Sequence Listing. Further, corresponding NHP homologues from other species are encompassed by the invention. any NHP encoded by the NHP nucleotide sequences described 30 above are within the scope of the invention, as are any novel polynucleotide sequences encoding all or any novel portion of an amino acid sequence presented in the Sequence Listing. degenerate nature of the genetic code is well known, and, accordingly, each amino acid presented in the Sequence 35 Listing, is generically representative of the well known nucleic acid "triplet" codon, or in many cases codons, that can encode the amino acid. As such, as contemplated herein,

the amino acid sequences presented in the Sequence Listing, when taken together with the genetic code (see, for example, Table 4-1 at page 109 of "Molecular Cell Biology", 1986, J. Darnell et al. eds., Scientific American Books, New York, NY, herein incorporated by reference) are generically representative of all the various permutations and combinations of nucleic acid sequences that can encode such amino acid sequences.

The invention also encompasses proteins that are 10 functionally equivalent to the NHPs encoded by the presently described nucleotide sequences as judged by any of a number of criteria, including, but not limited to, the ability to bind and cleave a substrate of a NHP, or the ability to effect an identical or complementary downstream pathway, or a change in 15 cellular metabolism (e.g., proteolytic activity, ion flux, tyrosine phosphorylation, etc.). Such functionally equivalent NHP proteins include, but are not limited to, additions or substitutions of amino acid residues within the amino acid sequence encoded by the NHP nucleotide sequences described above, but which result in a silent change, thus producing a functionally equivalent gene product. Amino acid substitutions can be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include 30 arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

A variety of host-expression vector systems can be used to express the NHP nucleotide sequences of the invention.

Where, as in the present instance, the NHP products or NHP polypeptides are thought to be soluble or secreted molecules, the peptide or polypeptide can be recovered from the culture media. Such expression systems also encompass engineered host

cells that express a NHP, or a functional equivalent, in situ. Purification or enrichment of NHP from such expression systems can be accomplished using appropriate detergents and lipid micelles and methods well known to those skilled in the art.

5 However, such engineered host cells themselves may be used in situations where it is important not only to retain the structural and functional characteristics of the NHP, but to assess biological activity, e.g., in drug screening assays.

The expression systems that may be used for purposes of 10 the invention include but are not limited to microorganisms such as bacteria (e.g., E. coli, B. subtilis) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing NHP nucleotide sequences; yeast (e.g., Saccharomyces, Pichia) transformed with recombinant 15 yeast expression vectors containing NHP encoding nucleotide sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing NHP sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant 20 plasmid expression vectors (e.g., Ti plasmid) containing NHP nucleotide sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3) harboring recombinant expression constructs containing promoters derived from the genome of 25 mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter).

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the NHP product being expressed. For example, when a large quantity of such a protein is to be produced for the generation of pharmaceutical compositions of or containing NHP, or for raising antibodies to a NHP, vectors that direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the *E. coli* expression vector pUR278 (Ruther et al., 1983, EMBO J. 2:1791), in which a NHP coding

sequence may be ligated individually into the vector in frame with the *lacZ* coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, 1985, Nucleic Acids Res. *13*:3101-3109; Van Heeke & Schuster, 1989, J. Biol. Chem. 5 264:5503-5509); and the like. pGEX vectors (Pharmacia or American Type Culture Collection) can also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. The PGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, Autographa californica nuclear polyhidrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in Spodoptera frugiperda cells. A NHP coding sequence can be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter). Successful insertion of NHP coding sequence will result in inactivation of the polyhedrin gene and production of non-occluded recombinant virus (i.e., virus lacking the proteinaceous coat coded for by the polyhedrin gene). These recombinant viruses are then used to infect Spodoptera frugiperda cells in which the inserted sequence is expressed (e.g., see Smith et al., 1983, J. Virol. 46: 584; Smith, U.S. Patent No. 4,215,051).

In mammalian host cells, a number of viral-based

30 expression systems may be utilized. In cases where an
adenovirus is used as an expression vector, the NHP nucleotide
sequence of interest may be ligated to an adenovirus
transcription/translation control complex, e.g., the late
promoter and tripartite leader sequence. This chimeric

35 sequence may then be inserted in the adenovirus genome by in
vitro or in vivo recombination. Insertion in a non-essential
region of the viral genome (e.g., region El or E3) will result

in a recombinant virus that is viable and capable of expressing a NHP product in infected hosts (e.g., See Logan & Shenk, 1984, Proc. Natl. Acad. Sci. USA 81:3655-3659). Specific initiation signals may also be required for efficient 5 translation of inserted NHP nucleotide sequences. These signals include the ATG initiation codon and adjacent sequences. In cases where an entire NHP gene or cDNA, including its own initiation codon and adjacent sequences, is inserted into the appropriate expression vector, no additional 10 translational control signals may be needed. However, in cases where only a portion of a NHP coding sequence is inserted, exogenous translational control signals, including, perhaps, the ATG initiation codon, must be provided. Furthermore, the initiation codon must be in phase with the 15 reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of 20 appropriate transcription enhancer elements, transcription terminators, etc. (See Bittner et al., 1987, Methods in Enzymol. 153:516-544).

In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or

25 modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the

30 post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper

35 processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include, but are not limited to, CHO,

VERO, BHK, HeLa, COS, MDCK, 293, 3T3, WI38, and in particular, human cell lines.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell 5 lines which stably express the NHP sequences described above can be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer sequences, 10 transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers 15 resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the NHP product. Such engineered cell lines may 20 be particularly useful in screening and evaluation of compounds that affect the endogenous activity of the NHP

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase

25 (Wigler, et al., 1977, Cell 11:223), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, 1962, Proc. Natl. Acad. Sci. USA 48:2026), and adenine phosphoribosyltransferase (Lowy, et al., 1980, Cell 22:817) genes can be employed in tk, hgprt or aprt cells,

30 respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler, et al., 1980, Natl. Acad. Sci. USA 77:3567; O'Hare, et al., 1981, Proc. Natl. Acad. Sci. USA 78:1527); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, 1981, Proc. Natl. Acad. Sci. USA 78:2072); neo, which confers resistance to the aminoglycoside G-418 (Colberre-Garapin, et al., 1981, J. Mol.

product.

Biol. 150:1); and hygro, which confers resistance to hygromycin (Santerre, et al., 1984, Gene 30:147).

Alternatively, any fusion protein can be readily purified by utilizing an antibody specific for the fusion protein being 5 expressed. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht, et al., 1991, Proc. Natl. Acad. Sci. USA 88:8972-8976). In this system, the sequence of interest is subcloned into a vaccinia 10 recombination plasmid such that the gene's open reading frame is translationally fused to an amino-terminal tag consisting of six histidine residues. Extracts from cells infected with recombinant vaccinia virus are loaded onto Ni<sup>2+</sup>·nitriloacetic acid-agarose columns and histidine-tagged proteins are 15 selectively eluted with imidazole-containing buffers. Also encompassed by the present invention are novel protein constructs engineered in such a way that they facilitate transport of the NHP to the target site, to the desired organ, across the cell membrane and/or to the nucleus where the NHP 20 can exert its function activity. This goal may be achieved by coupling of the NHP to a cytokine or other ligand that would direct the NHP to the target organ and facilitate receptor mediated transport across the membrane into the cytosol. Conjugation of NHPs to antibody molecules or their Fab 25 fragments could be used to target cells bearing a particular epitope. Attaching the appropriate signal sequence to the NHP would also transport the NHP to the desired location within the cell. Alternatively targeting of NHP or its nucleic acid sequence might be achieved using liposome or lipid complex 30 based delivery systems. Such technologies are described in Liposomes: A Practical Approach, New RRC ed., Oxford University Press, New York and in U.S. Patents Nos. 4,594,595, 5,459,127, 5,948,767 and 6,110,490 and their respective disclosures which are herein incorporated by reference in their entirety.

### 5.3 ANTIBODIES TO NHP PRODUCTS

Antibodies that specifically recognize one or more epitopes of a NHP, or epitopes of conserved variants of a NHP, or peptide fragments of a NHP are also encompassed by the invention. Such antibodies include but are not limited to polyclonal antibodies, monoclonal antibodies (mAbs), humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')<sub>2</sub> fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above.

The antibodies of the invention may be used, for example, in the detection of NHP in a biological sample and may, therefore, be utilized as part of a diagnostic or prognostic technique whereby patients may be tested for abnormal amounts of NHP. Such antibodies may also be utilized in conjunction with, for example, compound screening schemes for the evaluation of the effect of test compounds on expression and/or activity of a NHP gene product. Additionally, such antibodies can be used in conjunction gene therapy to, for example, evaluate the normal and/or engineered NHP-expressing cells prior to their introduction into the patient. Such antibodies may additionally be used as a method for the inhibition of abnormal NHP activity. Thus, such antibodies may, therefore, be utilized as part of treatment methods.

For the production of antibodies, various host animals may be immunized by injection with the NHP, an NHP peptide (e.g., one corresponding the a functional domain of an NHP), truncated NHP polypeptides (NHP in which one or more domains have been deleted), functional equivalents of the NHP or mutated variant of the NHP. Such host animals may include but are not limited to pigs, rabbits, mice, goats, and rats, to name but a few. Various adjuvants may be used to increase the immunological response, depending on the host species, including but not limited to Freund's adjuvant (complete and incomplete), mineral salts such as aluminum hydroxide or aluminum phosphate, surface active substances such as

lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and Corynebacterium parvum.

Alternatively, the immune response could be enhanced by combination and or coupling with molecules such as keyhole limpet hemocyanin, tetanus toxoid, diptheria toxoid, ovalbumin, cholera toxin or fragments thereof. Polyclonal antibodies are heterogeneous populations of antibody molecules derived from the sera of the immunized animals.

Monoclonal antibodies, which are homogeneous populations 10 of antibodies to a particular antigen, can be obtained by any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique of Kohler and 15 Milstein, (1975, Nature 256:495-497; and U.S. Patent No. 4,376,110), the human B-cell hybridoma technique (Kosbor et al., 1983, Immunology Today 4:72; Cole et al., 1983, Proc. Natl. Acad. Sci. USA 80:2026-2030), and the EBV-hybridoma technique (Cole et al., 1985, Monoclonal Antibodies And Cancer 20 Therapy, Alan R. Liss, Inc., pp. 77-96). Such antibodies may be of any immunoglobulin class including IgG, IgM, IgE, IgA, IgD and any subclass thereof. The hybridoma producing the mAb of this invention may be cultivated in vitro or in vivo. Production of high titers of mAbs in vivo makes this the 25 presently preferred method of production.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., 1984, Proc. Natl. Acad. Sci., 81:6851-6855; Neuberger et al., 1984, Nature, 312:604-608; Takeda et al., 1985, Nature, 314:452-454) by splicing the genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. Such technologies are described in U.S. Patents Nos. 6,075,181 and 5,877,397 and

their respective disclosures which are herein incorporated by reference in their entirety.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent 4,946,778; Bird, 1988, Science 242:423-426; Huston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; and Ward et al., 1989, Nature 334:544-546) can be adapted to produce single chain antibodies against NHP gene products. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide.

Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, such fragments include, but are not limited to: the F(ab')<sub>2</sub> fragments which can be produced by pepsin digestion of the antibody molecule and the Fab fragments which can be generated by reducing the disulfide bridges of the F(ab')<sub>2</sub> fragments. Alternatively, Fab expression libraries may be constructed (Huse et al., 1989, Science, 246:1275-1281) to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity.

Antibodies to a NHP can, in turn, be utilized to generate anti-idiotype antibodies that "mimic" a given NHP, using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, 1993, FASEB J 7(5):437-444; and

Nissinoff, 1991, J. Immunol. 147(8):2429-2438). For example antibodies which bind to a NHP domain and competitively inhibit the binding of NHP to its cognate receptor can be used to generate anti-idiotypes that "mimic" the NHP and, therefore, bind and activate or neutralize a receptor. Such anti-idiotypic antibodies or Fab fragments of such anti-idiotypes can be used in therapeutic regimens involving a NHP signaling pathway.

The present invention is not to be limited in scope by the specific embodiments described herein, which are intended as single illustrations of individual aspects of the invention, and functionally equivalent methods and components are within the scope of the invention. Indeed, various

modifications of the invention, in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the scope of the appended claims. All cited publications, patents, and patent applications are herein incorporated by reference in their entirety.

### WHAT IS CLAIMED IS:

10

 An isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence first
 disclosed in the NHP polynucleotide described in SEQ ID NO: 1.

- 2. An isolated nucleic acid molecule comprising a nucleotide sequence that:
  - (a) encodes the amino acid sequence shown in SEQ ID NO: 2; and
  - (b) hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.
- 3. An isolated nucleic acid molecule encoding the amino acid sequence described in SEQ ID NO: 2.

#### SEQUENCE LISTING

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## INTERNATIONAL SEARCH REPORT

Ir ational Application No PCT/US 00/33738

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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/11							
According to International Patent Classification (IPC) or to both national classification and IPC							
B. FIELDS SEARCHED							
Minimum documentation searched (classification system followed by classification symbols)  I PC 7 C12N							
Documentation searched other than minimum documentation to the extent that such documents are included. In the fields searched							
Electronic o	data base consulted during the international search (name of data t	pase and, where practical, search terms used	)				
EMBL							
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT						
Category *	Citation of document, with Indication, where appropriate, of the re	elevant passages	Relevant to claim No.				
X	DATABASE EMBL 'Online! EBI; Acc. No: ACO12228 22 October 1999 (1999-10-22) BIRREN B., LINTON L., NUSBAUM C. E.: "Homo sapiens chromosome 11 RP11-439A13 map 11, LOW-PASS SEQ SAMPLING" XP002163709 abstract	clone	1-3				
Furth	er documents are listed in the continuation of box C.	Patent family members are listed in	annex.				
*Special categories of cited documents:  'A' document defining the general state of the art which is not considered to be of particular relevance  'E' earlier document but published on or after the international filing date  'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another clation or other special reason (as specified)  'O' document referring to an oral disclosure, use, exhibition or other means  'P' document published after the international filing date of the art.  'S' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  '8' document member of the same patent family  Date of the actual completion of the international search  Date of mailing of the international search report							
Name and ma	ailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer Schwachtgen, J-L					